DOES NOT CIRCULATE

VOLUME 47 NUMBER 4 APRIL 1954

# PROCEEDINGS of the ROYAL SOCIETY OF MEDICINE

UNIVERSITY OF MICHIGAN
MAY 18 1954
MEDICAL LIBRARY

*Published for*
THE ROYAL SOCIETY OF MEDICINE, 1 WIMPOLE STREET, LONDON, W.1
*by*
H. K. LEWIS & Co. LTD., 136 GOWER STREET, LONDON, W.C.1
In U.S.A., GRUNE & STRATTON, INC., 381, FOURTH AVENUE, NEW YORK CITY
Monthly, 10s. 6d. net Annual Subscription, £6 6s. in the British Commonwealth, $19.00 in the U.S.A.

*All rights reserved*

# PATIENTS FIND IT VERY DELICIOUS

So often the sick, especially the very sick, find it difficult to enjoy a pleasant drink — but LUCOZADE invariably "fills the bill."

Patients of all ages find this sparkling presentation of glucose entirely delicious.

LUCOZADE in fact may be described as an almost perfect appetiser, sustaining in itself and a delightful stimulus to the desire for more solid food.

**Lucozade**
*the sparkling*
**GLUCOSE**
*drink*

# PROCEEDINGS *of the* ROYAL SOCIETY OF MEDICINE

ISSUED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE



HONORARY EDITORS

SIR HENEAGE OGILVIE  E. C. WARNER

EDITOR

J. M. BROWNE KUTSCHBACH

ROBERT COPE (Anæsthetics)
FRANCES GARDNER (Clinical)
J. B. BROOKSBY (Comparative Medicine)
D. I. WILLIAMS (Dermatology)
E. F. SCOWEN (Endocrinology)
IAN TAYLOR (Epidem. and Preventive Med.)
A. C. WHITE (Exper. Med. & Therap.)
L. CARLYLE LYON (General Practice)
H. M. SINCLAIR (History of Medicine)
W. A. MILL (Laryngology)
PHILIP ELLMAN (Medicine)
HELEN DIMSDALE (Neurology)
LESLIE WILLIAMS (Obstetrics and Gynæcology)
B. W. FICKLING (Odontology)
FREDERICK RIDLEY (Ophthalmology)
R. C. F. CATTERALL (Orthopædics)
G. H. BATEMAN (Otology)
D. MacCARTHY (Pædiatrics)
(Pathology)
W. S. TEGNER (Physical Medicine)
RONALD W. RAVEN (Proctology)
GERALD GARMANY (Psychiatry)
F. CAMPBELL GOLDING (Radiology)
D. H. PATEY (Surgery)
Surg. Cdr. J. L. S. COULTER (United Services)
A. CLIFFORD MORSON (Urology)

SECRETARY OF THE ROYAL SOCIETY OF MEDICINE

R. T. HEWITT



All communications concerning Editorial Business should be addressed to
THE HONORARY EDITORS, 1, WIMPOLE STREET, LONDON, W.1 (Tel.: LANGHAM 2070)



***In atonic constipation***

# PURSENNID

PURSENNID contains the pure Sennosides A & B of *Cassia angustifolia* in the form of their calcium salts.

PURSENNID taken at bed-time, exerts a gentle but effective laxative action on the following morning.

PURSENNID does not cause griping, cramps or colic owing to the fact that the active compounds are pure glucosides, constant in quality and potency, and the preparation is free from irritant impurities contained in crude senna preparations.

Tubes of 40 and 200 tablets.

*Schweiz. med. Wschr.*, 1941, **71**, 1093.
*Rev. méd. Suisse rom.*, 1941, **61**, 585.
*Amer. J. dig. Dis.*, 1945, **12**, 221.

SANDOZ

**SANDOZ PRODUCTS LIMITED**

*134, Wigmore Street,* *London, W.1*

## The professional touch . . .

There is that about the Jaguar which recommends it at once to the man of professional calling, and some measure of the high appreciation it inspires can be gauged from the frequency of its appearances in professional and diplomatic circles, not only in this country but throughout the world.

# JAGUAR

JAGUAR CARS LTD., *Coventry, England*
*London Showrooms:* HENLYS LTD.
*Devonshire House, Piccadilly, W.1*

*Grace . . . Space . . . Pace*

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

Vol. 47 No. 4 April 1954

## CONTENTS

Whole Proceedings Page

**Section of Pathology**
DISCUSSION: PATHOLOGICAL SEQUELÆ OF BURNS .. .. .. .. .. .. 225

**Section of Comparative Medicine with Section of Ophthalmology**
JOINT MEETING NO. 1
DISCUSSION ON PERIODIC OPHTHALMIA .. .. .. .. .. .. .. 233

**Books Recently Presented and Placed in the Society's Library** .. .. .. .. 240

**Section of the History of Medicine**
An Experiment of Galen's Repeated.—J. M. FORRESTER, M.A., B.M., B.Ch. .. 241

**Section of Laryngology**
MEETING AT THE ROYAL COLLEGE OF SURGEONS
DISCUSSION ON THE KERATOSES OF THE LARYNX .. .. .. .. .. 245

**Clinical Section**
*December* 11, 1953
CASES .. .. .. .. .. .. .. .. .. .. .. .. 255-258
*January* 8, 1954
CASES .. .. .. .. .. .. .. .. .. .. .. .. 258-264

*Continued overleaf*

**EMOTIONAL DISTURBANCE...**

A close association has been shown to exist between certain emotional disturbances and changes in gastric function. Increased acid secretion has been observed to follow emotional reactions of a combative nature and the importance of controlling gastric acidity in the management of peptic ulcer is widely recognised. 'Aludrox' Amphoteric Gel, buffers gastric acid to a pH of 3.5 to 4.0, at the same time providing a protective gel barrier over the surface of the ulcer. Healing is thus able to proceed whilst the risk of alkalosis is avoided and normal digestion is unimpaired.

ULCER EMOTIONS

**'ALUDROX'**
*Trade Mark*

Wyeth

*John Wyeth & Brother Ltd., Clifton House, Euston Road,* ***London, N.W.1***

## CONTENTS (*continued*)


Whole Proceedings Page

**Section of Physical Medicine**

DISCUSSION: ANTERIOR POLIOMYELITIS .. .. .. .. .. .. .. 265

**Section of Endocrinology**

CASES .. .. .. .. .. .. .. .. .. .. .. .. 275-280

**Section of Neurology**

*September* 1, 1953, *contd.*

JOINT MEETING WITH THE CANADIAN NEUROLOGICAL SOCIETY—AFTERNOON SESSION

Pain in Paraplegia—Clinical Management and Surgical Treatment.—E. H. BOTTERELL, M.D., J. C. CALLAGHAN, M.D., A. T. JOUSSE, M.D. .. .. .. .. .. 281

Loss of Visualization.—Sir RUSSELL BRAIN, D.M., P.R.C.P. .. .. .. .. 288

Basilar Artery Stenosis and Thrombosis.—J. L. SILVERSIDES, M.D.(Can.) .. .. 290

Pure Word Blindness Considered as a Disturbance of Visual Space Perception [*Abridged*].—J. PURDON MARTIN, M.A., M.D., F.R.C.P. .. .. .. .. 293

Post-encephalitic Mental Paroxysms.—J. ALLAN WALTERS, M.D., D.P.M., F.R.C.P. (Can.) .. .. .. .. .. .. .. .. .. .. .. 295

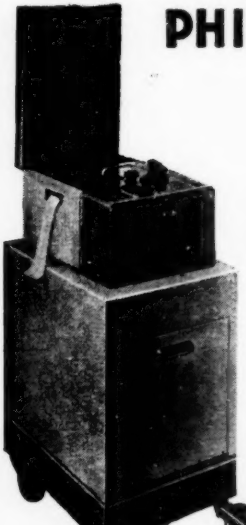
*November* 5, 1953

MEETING HELD AT THE NATIONAL HOSPITAL, QUEEN SQUARE, LONDON, W.C.1

CASES .. .. .. .. .. .. .. .. .. .. .. .. 296-300


*N.B.—The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.*

**Copyright:** The Society holds the copyright of all matter accepted for publication in the *Proceedings*. Requests for subsequent publication elsewhere should be made to the Honorary Editors. All papers, &c., presented at meetings (other than those which have been previously published) are held to be subject to the Society's copyright until a decision in regard to their publication has been made.

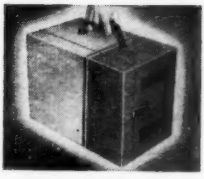



PHILIPS *Cardioluxe*

**DIRECT-WRITING**

Single Channel

**ELECTROCARDIOGRAPH**



**TRULY PORTABLE:**
*Weight, complete with all accessories,* ***only 31 lbs.***

ONE of the most outstanding instrument developments of recent years, the "Cardioluxe" Direct-Writing Electrocardiograph enables physicians to record all modern electrocardiographic leads accurately and instantaneously.

The extreme fidelity of this instrument, brought about by built-in standards of high accuracy, is such that it does not have to be compared with the so-called "standard" photographic apparatus. Complete freedom from interference guaranteed under all conditions. Write for full details.

**PHILIPS ELECTRICAL LTD.**

ELECTRO-MEDICAL APPARATUS · X-RAY EQUIPMENT FOR ALL PURPOSES · LAMPS & LIGHTING EQUIPMENT
RADIO & TELEVISION RECEIVERS · SOUND AMPLIFYING INSTALLATIONS

ELECTRO-MEDICAL DEPARTMENT, PHILIPS ELECTRICAL LIMITED, CENTURY HOUSE, SHAFTESBURY AVENUE, LONDON, W.C.2
(XP15C REV.)

# Section of Pathology

President—Professor G. PAYLING WRIGHT, D.M., F.R.C.P.

[*December* 15, 1953]

## DISCUSSION: PATHOLOGICAL SEQUELÆ OF BURNS

**Dr. Simon Sevitt**, Consultant Pathologist, Medical Research Council Burns Research Unit and Birmingham Accident Hospital:

*Local Vascular Changes in Burned Skin*

Clinically the local inflammatory changes after burning are manifest by redness and swelling of the skin. This communication is concerned with the increased permeability of the dermal capillaries and the changes in their blood flow.

*Outline of methods.*—Full details have been given elsewhere (Sevitt, 1949*a*, 1949*b*). Circular burns, 1 in. in diameter and of known temperature and duration were made with a constant temperature burning iron usually on the shaven abdomen of albino guinea-pigs. The animal's plasma was dyed by the injection of Evans blue or Brilliant Vital Red. Coloration of the burned skin is due to leakage of plasma albumin and indicates an increase of dermal capillary permeability (Fig. 2).

*The least severe burns causing an increase of permeability.*—In burns of the same duration, the appearance of dye occurs at and above a minimal burning temperature. For example (Fig. 1) in

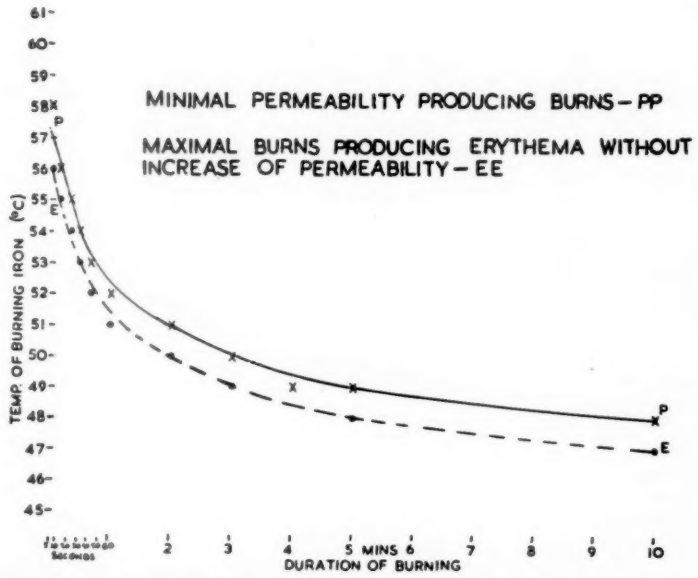



FIG. 1.—The minimal temperatures and periods of application of the burning iron which just produce an increase of permeability in the dermal capillaries. At and above curve PP an increase of permeability occurs; at and below EE erythema is the only evidence of burning. The curves were made by making many burns above, at and below the points recorded.

burns lasting 60 seconds this is 52° C., in five-minute burns it is 49°. Above curve PP an increase of permeability occurs, below EE erythema is the only visible evidence of burning. By extending PP to the right to obtain an infinitely prolonged burn, the lowest burning temperature which produces an increase of permeability is about 45°.

*Dermal threshold temperature.*—The temperatures in PP are those applied to the surface of the skin: during burning the temperatures in the dermis must be lower than these. By correlating the subdermal temperatures recorded during burning by Mendelssohn and Rossiter (1944), it has been shown that different burns, all of which just produce an increase of permeability, also produce similar subdermal temperatures. Thus the burn at 54° for 30 seconds produces a subdermal temperature of 41° to 44° in different animals: similarly, burning at 52° for 60 seconds produces a subdermal temperature of 41° to 45°. This suggests that a threshold temperature exists to which the dermal capillaries must be heated before they leak abnormally. In the prolonged burn at 45°, the subdermis reaches 41° to 42° and therefore within the range of 41° to 45° is the threshold temperature for increase of permeability.

*Delayed increase of permeability and delayed œdema.*—When Evans blue is injected before burning it usually stains the burned skin within a few minutes of burning. In less severe burns the dye may not appear for 30 to 60 minutes or longer. Experiments involving the injection of dye after burning, have shown that the delayed appearance of dye in these burns is mainly due to a delayed leakage of dye from the capillaries. By estimating the water content of burned skin, it has been shown that several hours' delay in œdema formation occurs in many burns. In severer burns, delayed permeability change and œdema formation occur in the subcutaneous tissues. The cause of this delayed permeability is obscure. It may be due to the diffusion of cell products released superficially and acting on the deeper capillaries but histamine release is not responsible (*vide infra*). Alternatively nervous influences may play a part. A fuller account of these experiments will be reported later.

*Burns on denervated skin.*—Does the permeability response on denervated skin differ from that on normal skin? Unilateral abdominal palsy and an area of anæsthetic abdominal skin was produced in guinea-pigs by unilateral section of the lower 1 or 2 thoracic and the upper 3 or 4 lumbar spinal nerves. Weeks later, Evans blue was injected and similar burns were made on the analgesic skin and on anatomically similar sites of the normal skin.

FIG. 2.—Burning denervated skin. Right-sided abdominal anæsthesia and palsy were produced in guinea-pigs by unilateral section of the thoracolumbar spinal nerves. Two months after operation similar burns were made on the right (anæsthetic) and left sides of the animal after intracardiac injection of Evans blue. In the photograph showing part of a guinea-pig's back, the results of two burns are recorded. The anæsthetic skin is outlined by skin pencil. The burn on the left side produced a circular blue patch of skin (P) corresponding to the site of application of the burning iron, indicating increased permeability of the dermal capillaries. However, dye did not appear in the homologous burn on the right side, the site of which is outlined by dots.

Many of the minor burns on the denervated skin did not produce a permeability change although similar burns produced the blue patches of increased permeability on the normal side of the animal (Fig. 2). In less minor burns, the permeability reactions were slight or indefinite on the denervated side but were definite on the normal side. Severer burns produced indistinguishable permeability reactions on both sides of the animal.

Analysis of the results showed that the time-temperature curve of the minimal burns producing a permeability increase on denervated skin lies at a level 2° to 3° higher than the curve for burns on normal skin (Fig. 3).

The difference between normal and denervated skin is due either to a raising of the permeability threshold temperature of the denervated dermis so that the dermal vessels cannot leak until a higher temperature is reached in the dermis; or alternatively to a lowered heat conductivity of the dermis so that a higher burning temperature is required to attain the normal dermal threshold for an increase in permeability.

*Capillary stasis in burned skin* (Sevitt, 1949*a*).—Many burns which show a permeability reaction to dye injected before burning, or some time after burning, show the reaction of stasis when the dye is injected later. A narrow coloured ring representing graded vascular damage surrounds the burn, but the site of application of the burning iron remains erythematous and does not blanch on pressure. Continuation of the dermal blood flow or development of statis within a period was demonstrated by the introduction of the red and blue dyes at different times—the double dye technique—and thus, the time limits of stasis involving the whole depth of the dermis were found. Stasis may set in hours, minutes or seconds after burning, the interval decreasing as the severity of burning increases until it develops within the burning period.

A dermal threshold temperature for stasis was postulated by correlating the minimal burning temperatures producing stasis (in burns of known duration), and the temperatures reached in the subdermis during burning. To produce stasis about four hours after burning, the dermis must reach a temperature of 47° to 48° during burning.

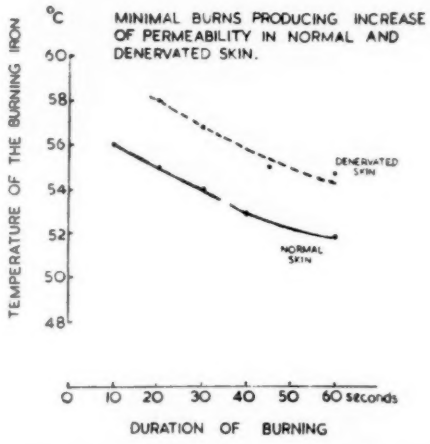



FIG. 3.—The minimal temperatures and periods of application of the burning iron which just produce an increase of capillary permeability in the denervated skin of the guinea-pig, compared to the minimal burns producing permeability increase on the normal side of the animals. The curve of burns on the denervated skin lies 2 degrees to 3 degrees higher than the burns on the normal skin.

*Failure of antihistamine drugs to influence the local vascular changes.*—The drugs Benadryl, Antistin and Anthisan were used in full, non-toxic dosage. Similar sets of burns varying in severity from minor to stasis-producing burns were made on antihistaminized and control guinea-pigs. Burn for burn similar permeability reactions or reactions of stasis occurred in the two sets of animals (Sevitt, 1949*b*). A burning experiment was performed on human volunteers, 4 taking Antistin and 4 taking dummy tablets. The inflammation, as measured by the clinical œdema and blistering produced, as well as the protein content and cellular exudate in the blister fluid, varied to the same extent in the volunteers taking Antistin as it did in the controls (Sevitt *et al.*, 1952). It was concluded that histamine release is not responsible for the inflammation in burned skin.

*Cortisone.*—In the guinea-pig experiments so far performed, similar dye reactions, burn for burn, have occurred in the controls and in the animals receiving cortisone, and quantitative skin water experiments indicate that cortisone has little, if any, influence on the degree of post-burn œdema.

Preliminary experiments with rabbits probably confirm the failure of cortisone to influence the permeability changes after burning but possibly indicate that cortisone may delay the onset of capillary stasis in the dermis. These experiments are not yet completed.

## REFERENCES

MENDELSSOHN, K., and ROSSITER, R. J. (1944) *Quart. J. exp. Physiol.*, **32**, 301.
SEVITT, S. (1949*a*) *J. Path. Bact.*, **61**, 427.
—— (1949*b*) *Brit. J. exp. Path.*, **30**, 540.
——, BULL, J. P., CRUICKSHANK, C. N. D., JACKSON, D. MACG., and LOWBURY, E. J. L. (1952) *Brit. med. J.*, ii, 57.

**Dr. W. J. H. Butterfield,** Medical Research Council's Clinical Research Unit, Guy's Hospital, London:

*The Endocrine Response to Burning Injury*

When cortisone and adrenocorticotrophic hormone (ACTH) became available, interest was aroused in the adrenocortical response to burns. By way of introducing this subject, we may review evidence for the release of adrenaline and ACTH, and I shall mention recent observations which broaden our ideas of the endocrine response to injury.

*The adrenaline response of the adrenal medullæ.*—Although this response has not been measured directly in burned patients—nor, for that matter, has any endocrine response—its occurrence is generally accepted. There is supporting evidence that fright and pain cause the release of adrenaline in animals (Elliott, 1912; Cannon, 1915). Other investigators have observed rises of blood pressure and blood sugar in burned animals; these changes can be attributed to adrenaline (Johnson and Blalock, 1931; Lambret and Driessens, 1937).

*The adrenocorticotrophic (ACTH) response of the anterior pituitary.*—Adrenaline released after burning may have a role in the release of ACTH from the anterior pituitary. McDermott *et al.* (1950), and Recant *et al.* (1950) have presented persuasive evidence that a rise in the level of circulating adrenaline causes an adrenocortical response mediated by the anterior pituitary.

*The adrenocortical response.*—A large number of steroids have been extracted from the adrenal cortex but Nelson *et al.* (1950) and Pincus *et al.* (1951) using perfused isolated mammalian adrenals find that ACTH causes the release principally of 11–17 hydroxycorticosterone (Hydrocortisone, Kendall's compound F.).

The effect of 1 gramme of this steroid given in diminishing daily doses over four days to a healthy young volunteer was investigated. He was kept lying in bed, immobilized in burn dressings. Compared with three control days there were: a prompt and profound fall of circulating eosinophils; increased daily urinary excretions of formaldehydogenic corticoids and 17-ketosteroids; decreased glucose tolerance; markedly positive sodium balance and negative potassium balance; less obvious fluid retention and increased urinary nitrogen excretion. (For methods, *see* Evans and Butterfield, 1951). These results confirm the findings of Fourman *et al.* (1950) and Conn *et al.* (1951).

*The similarity between the effects of 11–17 hydroxycorticosterone and those observed after burning injury.*—There was a close similarity between these effects of diminishing doses of 11–17 hydroxycorticosterone and measurements made after burning injury. Indeed, this resemblance was close both as to magnitude and timing when the results of the foregoing study were compared with measurements made during the first eight days after injury in a 30-year-old man who suffered a 30% burn. This patient showed an early profound depression of circulating eosinophils, and similar patterns to the volunteer as regards corticoid and 17-ketosteroid excretion, sodium and potassium balance and glucose tolerance. The findings with fluid and nitrogen balances were not so close, although, of course, the interpretations of all balance studies were complicated by treatment.

These investigations, and those in 18 other burned patients, suggest that there is an adrenocortical-like response to thermal injury, and that this could play an important part in producing many of the metabolic alterations seen in burned patients. Whether this response is due to increased adrenocortical activity or to decreased conjugation of adrenal steroids by the liver, or both, is not known.

*The variation in the magnitude of the adrenal response with the extent of burn.*—Analysis of the results over the first ten days after injury in 19 patients, of ages 4 months to 76 years and burns of 2–60%, showed highly significant correlations between the percentage body burned and the mean eosinophil count ($R = -0{\cdot}69$) and the mean daily corticoid excretion ($R = 0{\cdot}58$). The most plausible link between these variables is adrenal function. It would therefore seem that the extent of the burn affects the degree of adrenocortical response. The data from balance studies show the same trend, but are less amenable to mathematical analysis because of differences in treatment, age and sex.

*Other endocrine responses.*—Our day-by-day findings in the 19 burned patients suggest that endocrine systems other than the adrenals are involved. Theobald and Verney (1935) have shown that antidiuretic hormone is released after painful stimuli, and Barac (1946) has presented evidence for circulating antidiuretic substance in the blood of burned dogs. An antidiuretic response is probably an important factor after burning injury, and would explain discrepancies between electrolyte and fluid balance. Selye (1951) believes that growth hormone (S.T.H.) is released in response to injury, and causes the adrenal cortex to elaborate salt-retaining, desoxycorticosterone-like, steroids. Observations in one patient suggest that there was an increase of such steroids in the urine for a few days after injury. This mechanism would account for anomalies of electrolyte balance and of glucose tolerance. Romani (1952) reports that burning injury is followed by a thyrotrophic response, but Cope *et al.* (1952) have been unable to confirm this in burned patients.

## Conclusions

A study of burned patients strongly suggests that there are endocrine responses in the first week after burning injury. Although adrenocortical effects predominate, and vary with the extent of burning, there are reasons to believe that other endocrine systems are activated.

Now that powerful hormone preparations are available, the question arises as to whether the clinician should attempt to alter, or augment these endocrine responses. This should depend upon evidence of a faulty endocrine response; it should be borne in mind that death occurs from Cushing's disease as well as Addison's disease, from water intoxication as well as dehydration.

## REFERENCES


Barac, G. (1946) *C.R. Soc. Biol., Paris*, **140,** 1125.
Cannon, W. B. (1915) Bodily Changes in Pain, Hunger, Fear and Rage. New York.
Conn, J. W., Fajans, S. S., and Louis, L. H. (1951) *Science*, **113,** 713.
Cope, O., Nardi, G. L., Quijano, M., Rovit, R. L., Stanbury, J. B., and Wight, A. (1952) *Ann. Surg.*, **137,** 165.
Elliott, T. R. (1912) *J. Physiol.*, **44,** 374.
Evans, E. I., and Butterfield, W. J. H. (1951) *Ann. Surg.*, **134,** 588.
Fourman, P., Bartter, F. C., Albright, F., Dempsey, E., Carroll, E., and Alexander, J. (1950) *J. clin. Invest.*, **29,** 1462.
Johnson, G. S., and Blalock, A. (1931) *Arch. Surg., Chicago*, **23,** 855.
Lambret, O., and Driessens, J. (1937) *Rev. Chir., Paris*, **75,** 319.
McDermott, W. V., Fry, E. G., Brobeck, J. R., and Long, C. H. N. (1950) *Proc. Soc. exp. Biol., N.Y.*, **73,** 609.
Nelson, D. H., Reich, H., and Samuels, L. T. (1950) *Science*, **111,** 578.
Pincus, G., Hechter, O., and Zaffaroni, A. (1951) Proceedings of the Second Clinical ACTH Conference. Editor: J. R. Mote. London.
Recant, L., Hume, D. M., Forsham, P. H., and Thorn, G. W. (1950) *J. clin. Endocrin.*, **10,** 187.
Romani, J. D. (1952) *C.R. Soc. Biol., Paris*, **146,** 1685.
Selye, H. (1951) Personal communication.
Theobald, G. W., and Verney, E. B. (1935) *J. Physiol.*, **83,** 341.


**Dr. J. P. Bull,** Director, Medical Research Council Industrial Medicine and Burns Research Unit, Birmingham Accident Hospital:

### *Fluid and Electrolyte Exchange in Burns*

The basis of the main disturbance of fluid and salt balance in the burned patient is the increased permeability of the damaged local capillaries. This breakdown of the semipermeable barrier between the circulation and the remainder of the extracellular fluid results in an escape of fluid some of which collects in blisters, some leaves the body from raw surfaces and some collects in the extracellular space as œdema. In animal experiments it has been shown that a 50% burn may cause a loss of approximately one plasma volume of fluid (Leach *et al.*, 1943). Also, in experiments in which burned and unburned parts of the body were weighed, it has been demonstrated that the loss is primarily local into the burned tissues; the unburned tissues may even become lighter as a result of transfer of extracellular fluid. Corresponding to this the lymph flow from the burned limb increases in quantity and changes in composition from a low protein to a high protein content—approximately three-quarters of the normal plasma level. The exudate also contains its full complement of plasma electrolytes.

In the treated human patient further changes result from treatment. The loss of circulatory volume initially may be compensated by vasoconstriction but if, as in severe burns, leaking continues uncorrected, the diminished blood volume will cause tachycardia, hypotension and, if allowed to progress, death. Treatment with plasma or other appropriate colloid solution corrects hæmoconcentration and blood volume but to maintain this correction therapy must be continued so long as the leak lasts. This means that the volume of extracellular fluid is much enlarged, an effect which will be accentuated if much extra water or saline is used in treatment. Even when giving plasma the volumes required to maintain normal hæmatocrit values are of the order of a whole circulatory volume for a 40% surface area burn.

In view of these considerations and the dangers of overloading the extracellular space (Cope and Moore, 1947) the following appear to be rational principles of therapy:

(1) Colloid solution with full electrolyte complement, regulated in quantity by correction of hæmoconcentration, should be given to replace exudate and œdema. Reconstituted plasma has a protein concentration of about 5% which is close to the level in exudate. In view of the concurrent loss of red cells it is probable that this regime results in an under-correction of circulatory volume.

(2) Water and perhaps a small amount of salt are required to provide for losses by respiration, normal skin and urine. This total is of the order of 2–3 litres per 24 hours.

Further to this major exchange of fluid due to altered capillary permeability, there is some passage of sodium into the damaged cells and loss of potassium from them, but it is probable that the quantities involved are relatively small (Moore *et al.*, 1948).

One of the features of renal function following severe burns is a tendency to oliguria. In a recent study Dr. N. W. J. England and I have found that about 500 ml. urine per day can fairly easily be obtained during the first few days, but that neither increase of colloid input within orthodox limits nor moderate increases of sodium or water input can greatly increase this flow. This is particularly true of large burns. Many small burns do respond by excreting extra amounts of fluid given and a corollary is that if the urine output is good then fluid management is almost certainly satisfactory; but we have not had these high flows with the larger burns and have rather come to accept an oliguria of about 500 ml./day as a reasonable optimum. No great urea retention occurs with such flows, and any slight rises are subsequently quickly corrected. Our finding of good renal concentration in this series of cases did not suggest that tubular necrosis was present, and we consider that with modern treatment this is probably a rare complication. During the period of oliguria renal sodium retention usually occurs and studies have been made of the time and circumstances of onset and cessation of this retention. Serum sodium level characteristically declines during the period of retention and rises again after release.

Potassium exchange shows a relatively simple picture of sustained moderate renal output during the first few days resulting in slight negative balances if little potassium is given. The negative balance is readily corrected when full feeding commences a few days later. Serum potassium concentrations are, in the treated case, usually within normal limits. Abnormally high levels after burning appear to be rare; a commoner occurrence is a depressed serum level at about the fourth day if input has not by then recommenced.

The fluid and salt disturbance in burns is part of a general process in which local pathology and circulatory, renal and endocrine responses are involved. Many of the interrelations, particularly those concerned with circulatory volume changes, need further study.

## REFERENCES

COPE, O., and MOORE, F. D. (1947) *Ann. Surg.*, **126**, 1010.
LEACH, E. H., PETERS, R. A., and ROSSITER, R. J. (1943) *Quart. J. exp. Physiol.*, **32**, 67.
MOORE, F. D., EVANS, R. D., and BALL, M. R. (1948) *Ann. Surg.*, **128**, 266.

**Dr. Elizabeth Topley**, Medical Research Council Industrial Injuries and Burns Research Unit' Birmingham Accident Hospital.

### *The Fate of Red Cells following Burns*

The results, to be published elsewhere, on about 50 burns involving 5–60% of the body surface have served to emphasize the common hæmatological findings and the pathological processes that seem worthy of further investigation.

Simple budgeting of volumes of blood transfused and levels of the peripheral hæmoglobin or red cell count provided a crude picture of the degree of "red cell loss" at different stages of a burn. The average results were: from admission to first operation 38%; at excision and grafting operations 125%; between operations less than 20%; after operations less than 5%.

To the pathologist the most interesting "red cell loss" occurs from admission to the first grafting operation (usually two to three weeks). In this Unit the common practice during this time is to give a single blood transfusion equal to 40% of the blood volume. Isolated cases required repeated large blood transfusions. It is this rare type of case that has been most frequently reported in the past. It was not clear to us whether this single transfusion of 40% of the blood volume was required immediately after burning, or only when anæmia had developed. The patients investigated therefore included 12 given blood "early" in the shock stage, and 12 clinically comparable cases given blood "late" when the hæmoglobin had fallen to 80% or less of the expected normal for the age. Patients receiving blood "early" and "late" were found to be similar as regards the volumes of blood transfused and the peripheral red cell count at the time of operation. The calculated "red cell loss" was therefore also similar. The essential difference was that the patients transfused "early" went through a stage of a higher than normal red cell count, while those transfused "late" went through a stage of peripheral anæmia.

Plasma volume studies have been made using Evans blue, and red cell volume studies (32 tests) using the Ashby, or, less frequently, the $P^{32}$ method. The cause of the red cell loss was not a rise in plasma volume (10/10 plasma volume studies normal or below normal at the time of anæmia) but a fall in red cell volume (14/14 observations after the sixth day showed a red cell volume below the expected normal for the age of an order that would explain the fall in peripheral count). Although the red cell volume estimates during the first twenty-four hours after burning were often below the expected normal for the age, they were considerably higher than that found from the fourth day onwards. Comparison of total and transfused cell counts were made by differential agglutination tests with anti-M serum. The average finding was that transfused cells appeared to contribute to the loss of red cells to about the same degree as the patient's own cells.

During the first one or two weeks after a burn, when the fall in red cell volume appears to be the major cause of the burn anæmia, there were minor changes in blood films and reticulocyte counts. Hæmoglobin metabolism by the usual criteria was abnormal. The most dramatic change was a very variable erythrocyte protoporphyrin, which sometimes rose to two or more times the normal figure.

There have been many reviews of the causes of the anæmia of burns. That of Cope (1947) is perhaps the one which best expresses the current climate of opinions, and refers to the pioneer work in America which has emphasized the important role of fall in red cell volume affecting transfused as well as patient's cells (Moore *et al.*, 1946; Brooks *et al.*, 1951).

The present findings support the hypothesis that the major cause of the anæmia of burns before grafting is a disappearance of red cells. Although probably contributed to by the immediate effect of heat (Shen and Ham, 1943; Brown, 1946) and by hæmorrhage into exudate (Moore *et al.*, 1946) there remains a further unexplained loss of circulating cells that may prove to be the major cause of the anæmia and therefore appears worthy of further investigation. Although failure in the rate of red cell formation is probably one factor (Moore *et al.*, 1946; Cooray and De, 1949) even a complete failure could not explain the losses found.

The investigations by Miss S. Baar in this Unit suggest that the altered hæmoglobin metabolism as well as the unexplained disappearance of red cells is worthy of further investigation. The main finding is the raised erythrocyte protoporphyrin. The degree and acuteness of the changes suggests the possibility that more cells may be affected than could have matured during the time.

During the first two weeks after burning when red cell loss and abnormal hæmoglobin metabolism are most evident, there is also an enormous reticulo-endothelial response, with a very large outpouring of new leucocytes and other new cells to the burn area. There is, as also stressed by Cope (1947), some similarity between the anæmia of burns and the anæmia of acute infection. In both unexplained red cell disappearance involving a "curvilinear" disappearance of transfused red cells (Brown *et al.*, 1944) and an altered hæmoglobin metabolism (Cartwright *et al.*, 1946*a*, *b*; Grinstein *et al.*, 1948; Vaughan, 1948; James *et al.*, 1951) may be playing a part. To end with such a vague comparison stresses our ignorance of the mechansim of the fall in red cell volume in burns.

## REFERENCES


Brooks, J. W., Robinett, P., Largen, T. L., and Evans, E. I. (1951) *Surg. Gynec. Obstet.*, **93**, 543.
Brown, A. (1946) *J. Path. Bact.*, **58**, 367.
Brown, G. M., Hayward, O. C., Powell, E. O., and Witts, L. J. (1944) *J. Path. Bact.*, **56**, 81.
Cartwright, G. E., Lauritsen, M. A., Humphreys, S., Jones, P. J., Merrill, I. M., and Wintrobe, M. M. (1946*a*) *Science*, **103**, 72.
——, ——, Jones, P. J., Merrill, I. M., and Wintrobe, M. M. (1946*b*) *J. clin. Invest.*, **25**, 65.
Cooray, G. H., and De, S. N. (1949) *J. Path. Bact.*, **61**, 541.
Cope, O. (1947) *Surg. Gynec. Obstet.*, **84**, 999.
Grinstein, M., Silva, J. A., and Wintrobe, M. M. (1948) *J. clin. Invest.*, **27**, 245.
James, G. W., Purnell, O. J., and Evans, E. I. (1951) *J. clin. Invest.*, **30**, 181.
Moore, F. D., Peacock, W. C., Blakely, E., and Cope, O. (1946) *Ann. Surg.*, **124**, 811.
Shen, S. C., and Ham, T. H. (1943) *New Engl. J. Med.*, **229**, 701.
Vaughan, J. (1948) *Brit. med. J.*, i, 35.


Dr. **E. J. L. Lowbury**: Bacteriologist, Medical Research Council Industrial Injuries and Burns Research Unit, Birmingham Accident Hospital.

### *Infection of Burns*

Our knowledge of the bacteriology of burns is recent. Aldrich (1933) and Cruickshank (1935) isolated streptococci from burns, and such information was extended in the development of prophylaxis and chemotherapy (Colebrook *et al.*, 1944; Langohr *et al.*, 1947; Colebrook *et al.*, 1948). In superficial burns, it is doubtful whether healing is delayed by bacteria, but in burns with full-thickness skin loss they may cause obvious clinical infection, with prolonged inflammation, pain and delayed healing leading to severe contracture. Infection may spread locally and sometimes generally. Local infection may cause toxæmia.

Efforts to prevent these results have included early skin grafting, prophylaxis and therapy by antibiotics, aseptic dressing techniques, the use of air conditioning with filtered air for the dressing station, and other methods which have reduced but not eliminated infection (Colebrook *et al.*, 1948; Jackson *et al.*, 1951*a*, *b*; Lowbury, 1954).

*Local pathogenic effects of bacteria.*—Local infection is hard to recognize on a burn with much slough and exudate, but some assessment of the local pathogenic action of bacteria may be obtained from their interference with healing and skin grafting. As the presence of particular bacteria—even *Strep. pyogenes*—is not consistently associated with these effects, it is impossible to be certain whether, in a particular instance, delayed healing is the effect or cause of bacterial contamination.

A way of avoiding this difficulty is to suppress the growth of the organism in question by chemotherapy in approximately half of the burns and see whether these heal more quickly and take their grafts better than burns in which the organism is allowed to grow freely. For example, local polymyxin was found effective against *Ps. pyocyanea* and some coliform bacilli in a controlled prophylactic trial. Both grafting results and healing times were significantly better in those who had polymyxin, the average healing time of treated patients being three weeks shorter than that of the control patients (Jackson *et al.*, 1951*a*). We inferred that *Ps. pyocyanea* and other polymyxin-sensitive organisms were probably causing adverse local effects.

The local pathogenic action of *Strep. pyogenes* is more widely recognized than that of Gram-negative bacilli. It was confirmed in a comparison of graft failure (less than 80% take) in a series of patients whose burns were colonized by *Strep. pyogenes* at the time of operation (16/18—89%) and others in the same period whose burns had been cleared of *Strep. pyogenes* by oral Aureomycin (11/46—24%). Controlled trials of Aureomycin for *Staph. aureus* showed some evidence that staphylococci were also capable of preventing the take of skin grafts.

Evidence for the local pathogenic action of *Ps. pyocyanea* has come from another line of study. Pyocyanin was consistently shown to cause necrosis of human epithelial tissue culture at a concentration estimated from extraction of weighed gauze swabs to be exceeded in green exudate from some burns (Cruickshank and Lowbury, 1953).

*General pathogenic effects of bacteria.*—Aldrich (1933) put forward the hypothesis that infection plays an important part in the ætiology of shock. In the light of further studies, this view was rejected, but recent work (Fine, 1952) suggests that bacteria may cause shock to become irreversible. As treatment for shock improves, the role of bacteria in causing the pyrexia, wasting and occasionally death of badly burned patients who have survived the shock phase becomes of increasing clinical interest.

Cruickshank (1935) reported the isolation of *Strep. pyogenes* at post-mortem from the spleen of severely burned patients with the organism in their burns. In our experience of burned patients treated with antibiotics, blood culture has rarely been positive. The organism most commonly isolated from blood has been *Ps. pyocyanea*, which could sometimes be found in lesions of lungs, pleura and skin at post-mortem. An occasional source of septicæmia or pyæmia in the severely burned patient is septic thrombophlebitis starting in a vein used for administration of blood or plasma.

When the blood culture is negative, circulating toxins may be the cause of general symptoms. Attempts to demonstrate such a toxin in burned animals have given inconclusive results (e.g. Robertson and Boyd, 1923; Underhill and Kapsinow, 1931; Blalock, 1934). The appearance of antibodies produced in response to colonization by *Ps. pyocyanea* in burns (Fox and Lowbury, 1953) may result from the absorption of products of these bacteria. But the respective roles of tissue breakdown products and of bacterial toxins have not been defined, and further study on this problem is needed.

## REFERENCES


Aldrich, R. H. (1933) *New Engl. J. Med.*, **208**, 299.

Blalock, A. (1934) Quoted in Harkins, H. N. (1942) The Treatment of Burns. Springfield; p. 123.

Colebrook, L., *et al.* (1944) *Spec. Rep. Ser. med. Res. Coun.*, No. 249.

——, Duncan, J. M., and Ross, W. P. D. (1948) *Lancet*, i, 893.

Cruickshank, C. N. D., and Lowbury, E. J. L. (1953) *Brit. J. exp. Path.*, **34**, 583.

Cruickshank, R. (1935) *J. Path. Bact.*, **41**, 367.

Fine, J. (1952) In: First Conference on Shock and Circulatory Homeostatis. Editor: H. D. Green. Josiah Macy, Jr., Foundation, New York; p. 140.

Fox, J. E., and Lowbury, E. J. L. (1953) *J. Path. Bact.*, **65**, 519.

Jackson, D. M., Lowbury, E. J. L., and Topley, E. (1951*a*) *Lancet*, ii, 137.

——, ——, —— (1951*b*) *Lancet*, ii, 705.

Langohr, J. L., Owen, C. R., and Cope, O. (1947) *Ann. Surg.*, **125**, 452.

Lowbury, E. J. L. (1954) *Lancet*, i, 292.

Robertson, B., and Boyd, G. L. (1923) *J. Lab. clin. Med.*, **9**, 1.

Underhill, F. P., and Kapsinow, R. (1931) *J. Lab. clin. Med.*, **16**, 823.

JOINT MEETING No. 1

# Section of Comparative Medicine with Section of Ophthalmology

Chairman—HUMPHREY NEAME, F.R.C.S.
(President of the Section of Ophthalmology)

[*December* 16, 1953]

## DISCUSSION ON PERIODIC OPHTHALMIA

**Mr. M. Crawford** (Assistant Director, Commonwealth Bureau of Animal Health): *The Epidemiology and Causation of Recurrent Iridocyclitis of Horses*

This disease has a very long history, the earliest written description of it being by Vegetius in the fourth century A.D. It has many names such as periodic ophthalmia, recurrent ophthalmia, iridocyclitis, uveitis, moon-blindness, &c. Periodic ophthalmia is perhaps the name more generally used but I prefer to use recurrent iridocyclitis because (*a*) there is no definite fixed period between the recurrent attacks and (*b*) because the essential lesion is an iridocyclitis.

### EPIDEMIOLOGY

The disease has a wide geographical distribution. At one time it was a common disease in Great Britain but from about 1880 onwards the incidence very markedly declined and it is now comparatively uncommon. It was apparently a serious problem in the large coaching stables and in the stables of the old tramway horses. When it was common in Great Britain and Ireland the incidence was highest in low-lying ill-drained areas such as the Fen district and parts of Ireland.

The marked decline since about 1880 has been attributed by some to the introduction of the Horse Breeding Act which prohibited the use of stallions affected with a number of diseases, including disease of the eye, which were believed to be hereditary. Others attribute the decline to improvements in agriculture with drainage of swampy lands and better standards of hygiene in stables and farms. It is intriguing to note that the disappearance or rather the very marked decline in indigenous malaria in man in England dates from about the same time and has been attributed to similar factors.

This association with low-lying swampy areas has been noted in France, Germany and Holland.

At the present time the highest incidence of the disease seems to be in some of the Central European countries such as Yugoslavia and Austria and in the U.S.A. In the U.S.A. it has been estimated that 10% of the total horse population is affected, with incidences up to 30% in some areas. A peculiar and as yet unexplained fact is that the incidence in those parts of the U.S.A. which are on the western side of the Rocky Mountains is much lower than on the eastern side. In Canada the disease rarely occurs. Extensive outbreaks have been recorded in the Argentine. In Australia the disease is very rare, indeed some writers maintain that it is absent from that continent.

It occurs in India and in Indonesia but is not a serious problem in these countries. In S. Africa it is said to have been unknown before the Boer War during which it became a very serious problem in the horses of the British Army. After the war it apparently declined rapidly and disappeared.

As a rule the incidence is sporadic with a small number of cases in a stable and there is little evidence of infectiousness. Extensive outbreaks can and have occurred when large numbers of horses are collected together as for example during the Boer War in S. Africa and the First Great War in Flanders.

The clinical features and pathology of the disease will be dealt with by other speakers but there are two distinctive features which I would wish to stress before going on to discuss causation.

These are: (*a*) The manner in which acute attacks clear up only to recur after varying intervals of time, the interval being anything from one month up to a year or longer; (*b*) the sudden precipitous onset of the acute attacks.

## Causation

The older writers have stressed such factors as heredity, bad drainage, low standard of hygiene and ventilation in stables and, of course, the malign influence of the phases of the moon. Nutrition does not appear to have been considered important by them since cases occurred in well-fed horses as well as in poorly fed ones. The wolf tooth, a vestigial first premolar present in some horses, was also thought to be the cause.

### *Bacteria*

Many workers have searched for a bacterial agent and various cocci and bacteria have been isolated from time to time and have been claimed to be the cause. Among such workers was Robert Koch (1884), and during the 1914–18 War, Dalling, who isolated a coccobacillus from the optic nerve which at one stage he considered to be the cause. None of these agents, however, has stood the test of time. Although a severe ophthalmia may be produced by intra-ocular inoculation with a great variety of organisms none of them has been able to produce recurrent attacks.

Some years ago brucella, especially *Brucella suis* (Burky *et al.*, 1939; Jones and Maurer, 1942) was considered by some to be the cause. Here the evidence was mainly based on the demonstration of brucella agglutinins and opsonins in a considerable proportion of horses affected with recurrent ophthalmia. Dimock *et al.* (1948), however, were unable to set up the condition by inoculation of horses with virulent cultures of *Br. suis*. Moreover they were able to demonstrate that the sera of healthy horses contained brucella agglutinins just as frequently as did the sera of affected horses. Their results with 59 affected and 103 normal horses were positive reactions in 27% of healthy horses and in 23% of affected.

Davis *et al.* (1950) found no correlation between brucella agglutinins and the disease, nor were they able to isolate brucella from the eyes of affected horses. Brucella agglutinins are so commonly present in horses that Huddleston considers that no titre lower than 1 : 1,000 should be accepted as evidence of active infection in the horse.

In recent years leptospira have been suggested as the cause. Heusser (1948) in Switzerland appears to be the first to have suggested this and since his paper there have been a number of others. The Leptospira theory seems to be very much the same as the brucella, namely the finding of agglutinins in affected horses in higher proportion than in healthy ones. Leptospira do not seem to be a common cause of overt disease in horses, as they are in cattle and dogs, but inapparent infections seem to be very frequent judged by the high incidence of agglutinins that has been demonstrated in the course of surveys of blood from clinically healthy horses in various parts of the world, e.g. Switzerland (Heusser), U.S.A. (Yager *et al.*, 1950), Germany (Hartwigk, 1953) and also in Turkey, Australia and in Great Britain.

Heusser (1952) attempted to produce the disease by infecting 10 horses with *L. pomona*. He did produce an eye condition in two of his horses. The primary intravenous or intraperitoneal injection of cultures did not cause the disease but when after a variable period of time cultures were instilled into the conjunctival sac acute ophthalmia was produced and could be reproduced after an interval by the same procedure.

### *Viruses*

Viruses have been sought by a number of workers and Woods and Chesney (1930) claimed to have transmitted the disease by means of filtrates of affected ocular tissues injected intra-ocularly. This work has not been confirmed by others and it has been shown that an inflammatory condition of the eye superficially resembling recurrent ophthalmia could be produced using filtrates from healthy eyes. The essential feature of recurrence has not been produced by using filtrates.

### *Helminths*

Nematodes of various species have been put forward from time to time and of these there seems to be a reasonably good case for some of the Filarioidea. Two genera of this family are particularly worthy of attention.

The first is the setaria. This is a genus with a wide geographical distribution, species of which occur in horses, cattle and pigs. The adult worms are found moving about freely in the peritoneal cavity and the larvae in the blood stream. Transmission is by various species of mosquitoes. The larvæ

(microfilaria) normally present in the blood stream are capable on occasion of wandering into unusual situations and one of these is the aqueous humour of the eye.

The larvæ seem to be capable of partial development in the aqueous humour because specimens removed from the eye surgically are very much larger than larvæ, up to 2 in. in length, and are generally described by helminthologists as immature adults (the fully developed adult female is from 4 to 4½ in. long).

Such immature worms are not very uncommon in the eyes of horses in India and Ceylon and have been recorded in many other countries. I have seen a number of such cases in Ceylon. In India and Ceylon the usual practice is to have one syce for each horse; he practically lives with his horse and good syces are very observant. It is usually he who first draws the owner's attention to the presence of the worm in a horse's eye. The eye shows no departure from normal except that the worm can be readily observed swimming with an undulating movement in the aqueous humour. This stage with no visible damage to the eye generally continues for a considerable period but, unless the worm is removed surgically, sooner or later the horse is found one morning with an acute eye—conjunctivitis, œdema of the eyelids, photophobia, lacrimation, &c., quickly followed by opacity of the cornea. This condition may resolve or may progress to blindness. Such an attack is very similar to an attack of recurrent ophthalmia in its sudden onset and very acute nature. Whether recurrences of this condition occur I cannot say, for it was usual to operate as soon as the worm was noticed and before symptoms developed. The operation consisted in puncturing the cornea after local anæsthesia. In a successful operation the worm emerged in the flow of aqueous humour which followed the puncture.

The other genus is onchocerca. Species of this genus are found in horses and cattle in very many parts of the world including Great Britain. The adult worms are found in the ligamentum nuchæ and in the large flexor tendons of the limbs. The larvæ are found in large numbers in the skin but have also been found in the cornea and the sclerotic in cases of recurrent ophthalmia. Transmission is by certain species of culicoides (midges).

Krishna Iyer (1938) in India studied recurrent ophthalmia in two horse-breeding farms in the Punjab where a considerable incidence of the disease had occurred over a number of years. He was unable to demonstrate any bacterial or virus cause but on histological examination of the eyeballs and lacrimal glands of 6 cases he found larval nematodes in all of them in the substantia propria of the cornea and in the conjunctiva associated with eosinophilic and lymphocytic infiltration. A few microfilaria were also found in the lacrimal glands.

The microfilaria were examined by the helminthologist at Muktesar who stated that they appeared to be the larvæ of some species of onchocerca but that specific identification was not possible from sections.

More recently (1952) Böhm and Supperer working in Vienna examined material from the eyes of 19 cases of recurrent ophthalmia and found larvæ of *Onchocerca reticulata* in 14 of them. Adult onchocerca were present in the ligamentum nuchæ of 18—in the nineteenth horse the ligamentum nuchæ was not available for examination. In 6 healthy horses *O. reticulata* adults were present in the ligamentum nuchæ but no larvæ were found in the eyes.

In the affected eyes the microfilaria were found in the propria and under the epithelium especially at the corneal-sclerotic junction. Associated with the microfilaria there was perivascular infiltration of lymphocytes and polymorphs. Eosinophils were present but not particularly numerous. Small numbers of microfilaria were also present in the ciliary body. They estimated that as many as 150,000 microfilaria were present in one eye.

*Allergy*

During the recent war a commission under the direction of Campori was appointed to study the disease in horses of the Argentine artillery in which there had been a high incidence of the disease. The work was spread over five years and the commission had the advantage of having a large number of cases to study. The results were published in two reports in 1944 and 1945. They were unable to demonstrate any infective agent either bacterial or virus. All these artillery horses had been inoculated against three diseases with (*a*) a bacterial vaccine against strangles, (*b*) tetanus toxoid and (*c*) a chick embryo vaccine against equine encephalomyelitis. The commission found that they could provoke recurrences of the disease in affected horses by instillation into the conjunctival sac of peptone solutions. Following each artificially provoked recurrence there was a refractory period varying in length from about a month up to three or four months. The commission concluded that the horses had become sensitized to peptone as a result of the inoculations and that the disease was a manifestation of a local allergic condition of the eye.

That allergy plays an important part in the causation of the disease had been suggested previously by other workers, e.g. Von Scilly (1914), Manninger (1930), and by Bonaza and Merillat (1922), and the findings of the Argentine Commission to my mind lend very considerable support to this theory.

If allergy be the mechanism it is probable that it may be produced by more than one allergen. One could conceive that organisms causing mild or inapparent chronic infections and particularly organisms having a widespread geographical distribution and favoured by such conditions as swampy

ill-drained land and poor standards of hygiene would be the most likely to meet the case. It would also be probable that the occurrence of the disease would be favoured by conditions involving a concentration both of the infection and of horses giving opportunity for repeated reinfection.

It seems to me that either onchocerca or setaria and possibly leptospira could under certain conditions function as allergens and produce the disease. The wandering nature of the microfilarial stages of both onchocerca and setaria, together with the fact that during the course of their wanderings they not infrequently reach the tissues of the eye, gives them the opportunity of causing a local sensitization of the ocular tissues and for that reason I think they deserve much further study than they have as yet received.

REFERENCES


BÖHM, L. M., and SUPPERER, R. (1952) *S.B. öst. Akad. Wiss.*, **161**, 9.
BONAZA and MERILLAT, E. (1922) *Vet. Med.*, **17**, 213.
BURKY, E. L., THOMPSON, R. R., and ZEPP, H. M. (1939) *Amer. J. Ophthal.*, **22**, 1210.
CAMPORI, A. S., HARISPE, C., ECKELL, O. A., ORLIACQ, C., and GONZÁLEZ, B. (1944–1945) Oftalmia Periodica. Repts. Commission Argentine Dirección General of Remonta, Buenos Aires.
DALLING, T. (1919) *Vet. J.*, **75**, 16.
DAVIS, G. R., WOOD, R. M., GADD, J. D., and KENNEDY, R. E. (1950) *Cornell Vet*, **40**, 364.
DIMOCK, W. W., BRUNER, D. W., and EDWARDS, P. R. (1948) *Bull. Ky agric. Exp. Sta.*, No. 512.
HARTWIGK, H. (1953) *Tierärztl. Umsch.*, **8**, 154.
HEUSSER, H. (1948) *Schweiz. Arch. Tierheilk.*, **90**, 287.
—— (1952) *Schweiz. Arch. Tierheilk.*, **94**, 296.
IYER, P. R. K. (1938) *Indian J. vet. Sci.*, **8**, 3.
JONES, T. C., and MAURER, F. D. (1942) *J. Amer. vet. med. Ass.*, **101**, 248.
MANNINGER, R. (1930) *Arch. wiss. prakt. Tierheilk.*, **61**, 144.
MERILLAT, L. A. (1934) *J. Amer. vet. med. Ass.*, **84**, 100.
VON SCILLY (1914) Quoted by Merillat (1934).
WOODS, A. C., and CHESNEY, A. M. (1930) *J. exp. Med.*, **52**, 637.
YAGER, R. H., GOCHENOUR, W. S., and WETMORE, P. W. (1950) *J. Amer. vet. med. Ass.*, **117**, 207.


**Mr. R. C. Crowhurst** (Newmarket): *Clinical Aspects*

*Occurrence*

Periodic ophthalmia now occurs rarely and sporadically throughout Great Britain in all breeds of horses. It is more common in some districts, or even localized farms, than in others. It does not occur enzootically in England at present but years ago in crowded, insanitary stables many more cases were encountered.

It is very rare in foals and is most frequently seen in animals from 1 year up to 8 years old with perhaps the greater frequency in the younger animal with a descending frequency to the later age. From this age onwards it is extremely rare to encounter a fresh case.

*Course and Symptoms*

The clinical course is characterized by recurrent acute symptoms of iridocyclitis separated by quiescent periods. The first symptom, often unnoticed by attendants, is of increased lacrimation with overflow of tears down the face from one eye. It is extremely rare to see a primary attack simultaneously in both eyes. This is quickly followed by photophobia and congestion of the conjunctiva. In an acute primary attack, and in subsequent ones, the following symptoms occur: Marked myosis accompanied by either a cloudiness of the anterior chamber or a flocculent exudate, creamy, yellow or often olive-green in colour, which gravitates to the lower part of this chamber. Occasionally actual hæmorrhage also occurs into this chamber. It is noticeable that in the earlier attacks the cornea remains clear and it is only in subsequent very acute attacks that pericorneal vascular infiltration may be seen. Examination of the fundus at this stage is usually impossible. Intra-ocular tension is markedly decreased early in an acute attack and is readily demonstrated by palpation. Systemic disturbances during the acute phase, if they do occur, are so slight as to be practically unobservable.

These acute symptoms which may last from one to three weeks gradually resolve. The accumulation of pus-like exudate in the anterior chamber disappears often within a day or so. Although the eye may appear to regain a more normal transparency and appearance permanent changes usually persist, i.e. intra-ocular tension remains low and the eye appears shrunken causing deeper folds to appear in the upper lid. A degree of myosis usually remains and the iris loses some of its normal bluish-brown colour and takes on a somewhat "wrinkled dead leaf" appearance. Irregularity of the outline of the pupil often appears owing to posterior synechiæ and parts of the iris may even become detached on to the anterior surface of the lens. The eye settles down in this quiescent state but almost certainly other attacks will occur in the affected eye at variable intervals of a few weeks to many months. It may well be that attacks will occur in the other eye but not necessarily coinciding with attacks in the already affected eye. In our experience a little less than 50% of horses affected became so in both eyes but the period before the second eye is first attacked may be prolonged and in fact I can recall one horse which first became affected in the second eye two years following the initial attack in the first eye.

Following one or a series of acute attacks permanent degenerative changes are taking place within the structures of the eye, e.g. synechiæ, progressive opacity of the lens, resulting in complete and permanent blindness. There comes a time when acute attacks cease to occur and eventually greater shrinkage in the size of the eye takes place accompanied by markedly irregular opacities and pigmentation of the cornea. The general health and condition of the animal is unimpaired and provided the other eye remains free it can lead a normal and useful life.

*Diagnosis*

Diagnosis can only be made on observation of symptoms in acute cases and by the chronic lesions found in quiescent ones. It is only in initial attacks that periodic ophthalmia may be confused with slight traumatic injuries but in the latter cases the lesions are usually confined to the cornea. There is no diagnostic laboratory test.

*Prognosis*

Prognosis is very grave in the vast majority of cases. Blindness in the affected eye will sooner or later occur and in a little under 50% of cases the second eye also becomes similarly involved. Very rarely Reynolds has seen spontaneous recovery in eyes which showed typical lesions following an acute attack.

*Treatment*

Various treatments have been tried according to the differing theories of ætiology, but so far no definite success can be claimed for any. Atropine reduces the danger of development of synechiæ but it does not arrest the course of the disease. Addition of riboflavin to the diet also does not influence the course of the disease in the affected eye, nor does it, in our experience, prevent the second eye from becoming involved. Various antibiotics and antihistamines have given disappointing results.

*Some Points to be Considered in Ætiology*

(1) No similar disease occurs in any other animal.

(2) The variable periodicity of acute attacks is such a strange feature.

(3) Heredity appears to play no part but the disease seems to be more a matter of environment, e.g. out of a group of 32 Arab horses imported since the war into England from Iraq, where periodic ophthalmia is extremely rare or does not occur, 3 have since developed typical symptoms. Also in West U.S.A. the disease is rare whereas in the East it is not uncommon.

(4) In England at present the disease occurs only sporadically but when large numbers of horses are gathered together under possibly unfavourable conditions then the disease takes on, it has been recorded, epizootic proportions.

(5) No infective organisms, virus or bacteria, have consistently been isolated from affected eyes nor has it been possible regularly to transmit the disease by inoculation of material collected from affected eyes or by live cultures.

(6) It is difficult to understand nutritional deficiencies being responsible because it occurs not only in stabled horses but also in horses living under the best natural conditions at grass during the summer months.

(7) Wandering helminth parasites cannot be incriminated but it has been suggested that toxins absorbed from migrating larvæ may be responsible. If this were so, one would expect a greater incidence in these islands where infestation of ascaris and strongylus larvæ is constant and often heavy, and usually highest in foals. Parasitism could hardly account for sudden epizootic-like outbreaks.

(8) It has been suggested that periodic ophthalmia results from sensitization due to some foreign proteins. This theory could account for the sudden onset in many cases where horses are living in large groups when foraging conditions are not of the best and forage, &c., may be mouldy. This theory could also account for the fact that periodic ophthalmia occurs mostly in temperate climates and not where dry, bright, good harvesting conditions prevail. It has recently been shown by Alstron and Lauritzon (1953, Proceedings, International Veterinary Congress, Stockholm) that some forms of emphysema of horses' lungs are due to hypersensitivity to aspergillus moulds which only produces the condition when horses come into immediate contact with infected hay.

**The Chairman** (Mr. Humphrey Neame) discussed the role of vitamin $B_2$ (riboflavin) in periodic ophthalmia in horses with reference to other deficiencies in plants, animals and man. His paper will be published elsewhere.

**Dr. Norman Ashton** (Institute of Ophthalmology, London):

*Pathology*

The histopathology of periodic ophthalmia has been well described by Jakob (1927), Woods and Chesney (1930), Schlotthauer (1933, 1938) and particularly by Jones (1942). As Jones has pointed out, it is necessary to consider the pathological changes in relation to the three clinical phases of the disease; the *acute*, in which active inflammatory signs are present in the eye, the *quiescent*, wherein the acute reaction has temporarily abated and the *old*, in which the acute reaction has entirely subsided.

In the *acute stage*, according to Jones, who examined as many as 18 eyes in this phase of the disease, the cornea and retina are consistently normal and the pathological changes are confined to the anterior uvea and adjacent structures. The iris and ciliary body are extensively infiltrated with lymphocytes, and a fibrinous cellular exudate exudes from the tissues to appear on the surface of the iris, in the posterior chamber, on the lens capsule, and it may extend into the anterior vitreous. Aggregations of inflammatory cells are seen in the region of the ora and within the ciliary epithelium. Thus the initial picture is simply that of an acute iridocyclitis. Hyphæma and hypopyon may both occur. At the same time there is congestion of the conjunctiva and swelling of the lids where large subepithelial lymphocytic aggregations appear. It is to be remembered, however, that lymphoid nodules occur normally in the conjunctival stroma of the equine eye, but Jones was of the opinion that they became hyperplastic in periodic ophthalmia. Nevertheless, despite the early symptoms of swelling of the eyelids, there appears to be no other histopathological change within the lid tissues.

The degree of histological changes to be discerned in the *quiescent stage* depends largely upon the number of recurrences which have taken place; indeed they may be so slight as to be easily overlooked. The presence of circumscribed lymphoid nodules in the iris and ciliary body is characteristic and they are usually in the neighbourhood of small blood vessels—these, however, are merely aggregations of lymphocytes and are not true lymph follicles in that they have no germinal centres (Woods and Chesney, 1930). A cyclitic membrane, heavily infiltrated with small round cells may be present and inflammatory cells may be seen in the uveal meshwork. Peripheral anterior and posterior synechiæ develop and the lens capsule thickens. Diffuse or focal aggregations of lymphocytes may frequently be seen on the surface and within the optic nerve head, but the retina itself is not usually affected until late in the disease when the eye has been subjected to repeated acute attacks; it then undergoes exudative and degenerative changes, and retinal detachment ensues. Cellular infiltration of the intravaginal space of the nerve sheath may be present. The cornea now shows evidence of a keratitis, being invaded with inflammatory cells and deep and superficial vessels.

In the *third and final stage* the changes are those of atrophia bulbi. There is secondary cataract with calcification of the lens capsule and total detachment and complete degeneration of the retina. The uvea is sclerosed and the walls of the blood vessels thickened.

In summarizing these pathological lesions, Jones emphasized that the disease is primarily a recurring, acute, fibrinolymphocytic iridocyclitis which gradually progresses to a chronic degeneration of all the intra-ocular structures.

The conclusions to be reached from histological findings alone are necessarily limited, but it would appear that the microscopical picture of this disease differs little from many cases of recurrent iridocyclitis in the human, where the ætiology is equally obscure and an even more pressing problem. It is doubtful whether there are any specific histological features in periodic ophthalmia, for all of the pathological changes, including the lymphocytic foci, are to be found in human iridocyclitis. The two problems differ, however, in that it is often impossible in human cases to discover any convincing explanation for the uveal inflammatory reaction, whereas in the horse it is difficult to select the correct ætiology from the large number of possibilities which present themselves. Are we right in searching for a single ætiology? Certainly the microscopical picture does not exclude the disease being due to a variety of ætiological agents; indeed periodic ophthalmia may, in fact, have several different causes. The histopathology is not inconsistent with an allergic, leptospira or virus ætiology and the lymphoid follicles are particularly reminiscent of the ocular reaction in brucellosis.

On the other hand it is not in harmony with some of the agents which have been suggested. Thus the fact that the corneal involvement appears to be of a secondary rather than a primary character does not suggest that any vitamin or protein deficiency is likely to be directly involved. Nor is the inflammatory reaction of the type associated with helminthic parasitic larvæ or with invasion by pyogenic organisms.

Unfortunately simple histological examination is unlikely to advance our knowledge much beyond this point and, as in the problem of toxoplasma infection in the human adult, cultures and animal inoculations of fresh uveal tissue from early cases of periodic ophthalmia have a better prospect of yielding further information if the disease is due directly to a living organism. Meanwhile this condition is better called recurrent iridocyclitis and we should bear in mind that it may well not be a single disease entity.

I am indebted to Mr. Arthur L. McCurry and Dr. Alan C. Woods who have kindly assisted me by the provision of material.

## REFERENCES

JAKOB, H. (1927) *Ergebn. allg. Path. path. Anat.*, **21**, 77.
JONES, T. C. (1942) *Amer. J. vet. Res.*, **3**, 45.
SCHLOTTHAUER, C. F. (1933) *N. Amer. Vet.*, **14**, 18.
—— (1938) *Vet. Med.*, **33**, 210.
WOODS, A. C., and CHESNEY, A. M. (1930) *J. exp. Med.*, **52**, 637.

**Professor James McCunn** said that many of the pathological processes and reactions in an animal's eye were similar to those observed in a human eye.

Competent research workers had studied periodic ophthalmia for many years. Most of that work had been in the bacteriological field. They had not found any organism which could be described as being consistently the cause of the trouble. Therefore he thought that it was reasonable to forgo the idea of some bacterial cause.

He was inclined to the opinion that periodic ophthalmia was in some way associated with a vitamin deficiency: he would say vitamins A, B, C and D. Clinically he divided the cases as follows: Cornea, anterior chamber and aqueous humour: A, B and probably to some extent D. The lens and the vitreous humour: vitamin C.

He was sure that simple corneal ulcer had a deficiency background. Some minor injury could precipitate the lesion. A simple corneal ulcer in a dog could be resolved in three weeks if the animal be given cod-liver oil internally.

In periodic ophthalmia in the horse he relied upon cod-liver oil and yeast given in the food, plus the topical application of cod-liver oil mixed in equal parts with colloidal iodine oil. He had found that cod-liver oil which had gone slightly rancid gave best results on topical application.

**Mr. M. Crawford,** in reply to a question regarding cattle and camels, said that so far as he knew there was no disease in these animals analogous to the recurrent iridocyclitis of horses. Both cattle and camels were subject to an infectious conjunctivitis and keratitis and that condition was sometimes loosely called ophthalmia.

As for deficiency of riboflavin and other vitamins, it was difficult to imagine conditions under which horses—particularly thoroughbreds in good stables—would be getting a diet which would be markedly deficient in riboflavin or any other vitamin. Even if the diet contained insufficient vitamin B the microflora of the capacious cæcum of the horse would probably produce sufficient of the vitamin B-complex to supply requirements. The only vitamin B deficiency in the horse which was well established occurred in horses poisoned with bracken. This was not the result of a deficiency in the diet but arose because bracken contained anti-thiaminase which destroyed thiamin. The syndrome of bracken poisoning in horses was well known and in that condition the eyes were not affected. Further, bracken poisoning could be cured by administration of large doses of thiamin while such treatment was of no value in recurrent ophthalmia.

He had hoped that in the discussion some of their medical colleagues would have spoken of the ophthalmia in man in Africa and Mexico which occurred in areas where onchocerciasis was endemic. In the account of this human condition given in Manson-Bahr's textbook of Tropical Diseases (Manson's Tropical Diseases. Edited by Manson-Bahr, P. H. 13th Edit. London, 1950) he had been interested to read that the skin nodules which occurred showed exacerbations from time to time and that these exacerbations had, by the inhabitants of these districts, been attributed to the phases of the moon, an interesting analogy with the old belief that recurrent iridocyclitis of the horse, or "moon blindness", was related to the phases of the moon.

It seemed to him that allergy was the most likely mechanism to explain the sudden onset and the tendency to recurrence, and the pathology was in line with such a concept. Since allergic manifestations are such a feature of filarial diseases of man, he considered that the role of nematodes such as onchocerca and setaria required much closer study in the elucidation of the cause of recurrent iridocyclitis of the horse.

**Mr. R. C. Crowhurst** said that periodic ophthalmia occurred not only in horses but in mules as well, though to a lesser degree. He did not know about donkeys; he had never seen a case in a donkey, but then he had not seen many donkeys. Riboflavin deficiency could occur but he was not prepared to say that it occurred among horses which ran out to grass, nor indeed that it occurred in the case of horses kept in well-run stables. The results of adding riboflavin to the diet as suggested by Jones *et al.* (1945) had been disappointing. In practically all cases in which they had put on the yeast supplement or actual riboflavin with the diet they had found a certain development of lesions in the other eye. Although these animals were kept on this supplemented diet he could not say that the result was very satisfactory.

One speaker had suggested that cortisone might be useful. They had not had cortisone available as yet for treatment, but they would like to be able to use it. There were reports (Ohlson, 1953) from Sweden that cortisone had been used in this condition and had brought about quite rapid recovery, but he did not know whether it was claimed that cortisone prevented recurrence. He would stress that in their experience—in his own personal experience particularly—he had never seen one case of definite periodic ophthalmia which had resolved completely. Certainly he had not seen a case in which recurrent attacks had not taken place. At the same time he was bound to add that his senior partner, Mr. E. B. Reynolds, was confident that he had seen one or two cases which had resolved completely.

## REFERENCES

JONES, T. C., MAURER, F. D., and ROBY, T. O. (1945) *Amer. J. vet. Res.*, **6**, 67.
OHLSON, L. (1953) Personal communication.

## BOOKS RECENTLY PRESENTED AND PLACED IN THE SOCIETY'S LIBRARY

**Aberle (S. B. de), and Corner (G. W.).** Twenty-five years of sex research: history of the National Research Council Committee for Research in Problems of Sex, 1922–1947. pp. 248. Philadelphia and London: Saunders. 20s. 0d. 1953.

**Albahary (C.).** Maladies médicamenteuses d'ordre thérapeutique et accidentel. pp. 751. Paris: Masson. Fr. 5,000. 1953.

**Barton-Wright (E. C.).** Practical methods for the microbiological assay of the vitamin B complex and essential amino acids. pp. 58. London: Ashe Laboratories. 1946.

**Congreso Panamericano de Pediatría.** Congresos de Pediatría de Montevideo. 3 Congreso Panamericano de Pediatría . . . 3 Congreso Sudamericano de Pediatría . . . 2–8 diciembre, 1951. Tomo **1.** pp. 794. Montevideo. 1953.

**Gilmour (W. S.).** Tuberculosis in the West Indies: report on sociological and clinical survey. pp. 221. London: National Association for the Prevention of Tuberculosis. 1946.

**Haas (S. V.).** Golden Jubilee world tribute to Dr. Sidney V. Haas. In honor of his pioneering contribution to celiac therapy and the treatment of the hypertonic infant, and of the completion of his fiftieth year of medical practice. pp. 35. New York: Committee Golden Jubilee Tribute. 1949.

**Hyman (H. T.).** Handbook of differential diagnosis. pp. 716. Philadelphia, etc.: Lippincott. 55s. 0d. 1953.

**Leyton (R. N. A.).** Migraine and periodic headache: a modern approach to successful treatment. 2nd edit. pp. 128. London: Heinemann. 12s. 6d. 1954.

**Medicine Illustrated.** Spot diagnosis. Vol. **1.** pp. 128. London: Harvey & Blythe. 7s. 6d. 1954.

**Petrie (G. F.), ed.** British medical science and practice: an anthology. pp. 172. London, New York, etc.: Longmans. 15s. 0d. 1953.

**Read (G. D.).** L'accouchement sans douleurs. pp. 210. Paris: Colbert. Fr. 900. 1953.

**Read (G. D.).** Gjør fødselen letter. pp. 108. Oslo: Fabritius and Sønner. 1953.

**Read (G. D.).** Moeder worden zonder vrees. pp. 173. Amsterdam: Scheltema and Holkema. Fl. 4.75. 1949.

**Read (G. D.).** Mutterwerden ohne Schmerz. 2te Aufl. pp. 299. Hamburg: Hoffman & Campe. 1953.

**Read (G. D.).** Den naturlige fødsel. pp. 258. Copenhagen: Arne Frost-Hansen. 1949.

**Read (G. D.).** Vi venter et barn. pp. 87. Copenhagen: Hirschsprung. 1953.

**Saupe (E.).** Die Röntgenbildanalyse: eine röntgendiagnostische Anleitung für Studierende und Ärzte. Bearbeitet von W. E. Baensch. 2te Aufl. pp. 244. Stuttgart: Thieme. D.M. 39. 1949.

**White (H. P. Winsbury-).** Stone in the urinary tract. 2nd edit. pp. 328. London: Butterworth. 63s. 0d. 1954.

**Winterton (W. R.).** Aids to gynæcology. 11th edit. pp. 196. London: Baillière, Tindall and Cox. 1953.

# Section of the History of Medicine

President—The Right Hon. Lord WEBB-JOHNSON, G.C.V.O., C.B.E., D.S.O., T.D., M.B., F.R.C.S., LL.D.

[*January* 6, 1954]

## An Experiment of Galen's Repeated

By J. M. FORRESTER, M.A., B.M., B.Ch.
*Magdalen College, Oxford*

GALEN lived from about A.D. 130 to 200 [1], and an account of his life and place in medical history has been given recently by Singer [2]. The experiment of his with which this paper deals is concerned with the means by which the arterial pulse is conducted. It is described towards the close of his treatise *An in Arteriis Natura Sanguis Contineatur* [3], which is believed to have been written between A.D. 169 and 180 [4]. In order to understand the point of this experiment, it is necessary to follow the argument of this brief treatise, leading up to the experimental details.

The argument discusses the question whether there is in fact any blood in the arteries. It was a common belief in the ancient world that the arterial system was filled, not with blood, but with air, or, more precisely, with pneuma. Galen held that it was filled with a mixture of blood and pneuma, and naturally first points out that a cut artery bleeds. This fact was familiar to anyone doing experimental work on animals, and capable of identifying arteries with precision, as Galen was. Furthermore, no discernible emission of pneuma from the artery occurs.

These observations, so conclusive to modern eyes, were not in themselves sufficient to establish Galen's case against his opponents. A rival theory was held by the Erasistrateans, a recognized school of medical thought in Galen's day, who followed Erasistratus, the great anatomist of Alexandria (*c.* 280 B.C.). The gist of this theory was that only after the pneuma had been ejected through a wound did blood enter the arterial system at all. The symptoms and signs of its entry, alleged this school, were flushing, a feeling of heat, and cardiac excitement.

It is of interest to note that this rival school was compelled to deduce the existence of tiny invisible channels, by which the blood from the venous system could make its transit to the arterial system whenever a wound occurred. These channels bear a remarkable resemblance to the capillaries as known to us. It is also noteworthy that the Erasistrateans were able by their apparently far-fetched theory to account for two contrasting simple observations: first, that cut arteries bleed, and second, that nevertheless the arterial system contains practically no blood as a rule when opened after death.

They were, however, placed in an obvious difficulty by Galen's point that no emission of pneuma is perceptible when an artery is cut. Their rejoinder, absurd on casual consideration, was that such an emission did occur, but with lightning speed, and imperceptibly. To comprehend the reason for this rejoinder, and for the serious consideration Galen paid to it, one must digress briefly into the already long intellectual history of pneuma.

That history may begin from the Ionian sage Anaximenes (610–545 B.C.), who in the dawning of physical speculation held that air was the primary substance, from which by processes of condensation, expansion, and differentiation all phenomena arose. For this substance he seems to have used the words air, pneuma and wind synonymously. In its long later development, pneuma in various guises appears to serve as a precarious bridge between mind and soul on the one hand, and matter on the other—to attempt a translation into much more modern terms. Hence it partakes now more of the nature of one end of the bridge, now more of the nature of the other. Sometimes it seems equivalent to air or gas, sometimes it acquires the active but insubstantial qualities of mind. It entered into anatomy with Alcmaeon (*c.* 500 B.C.), a shadowy figure, who is believed to have dissected animals, and who looked upon the nerves and arteries as channels of pneuma, and the brain as containing a specially fine form of pneuma, the psychic variety. Thereafter the word had a long and chequered history in physics, metaphysics, and medicine [5].

But enough has already been said to show how a pneuma capable of emerging instantaneously and unperceived from a wounded artery was a conception founded on a long history of changing ideas, rather than being the recourse of a debater reduced to absurdities. As such, it demanded an answer. Pneuma, hard pressed in its more material aspects, was taking refuge in its metaphysical fastnesses, from which Galen had to dislodge it.

Galen sets out to do so in the appropriate terms. What, he asks, drives the pneuma out from a wound? Can it be some necessity of its own nature? For such a necessity to operate, apparently the pneuma would have to be either thinner or hotter than the surrounding air. But pneuma is not thinner, says Galen, for it is itself made from air by associating with the lungs and heart, and these, being damp organs, would be bound to thicken the air. Anyway, if pneuma were so thin, it could not be contained by the arterial walls, but would permeate out of them. Secondly, were the pneuma

hotter, it ought apparently to be perceptible as it emerges, like vapour, or like air emerging from a chest wound; and even the smallest wounds of arteries do not show the exit of the pneuma enough to make it visible.

A further objection made by Galen is this: the Erasistrateans maintained that the blood entering the arterial system after a wound did so first into the most peripheral arteries. On this assumption presumably before blood can emerge from a wound of a large artery at all, the total amount of pneuma in the whole system must have been lost through the wound. If all the pneuma is lost, and especially when its inmost shrine, the left ventricle, is filled with blood, the animal must be dead, even before any blood at all is actually shed from the wound—because pneuma in its metaphysical aspect is wrapped up with life itself.

Passing lightly over this secondary objection, Galen returns us again to the question of what ejects the pneuma from the wound. If it is not ejected by the necessity of its own nature, can the heart be a pneuma pump, and pump it out through the wound? His ingenious answer is this: either arteries can collapse entirely, like veins, so that their lumen is obliterated, or they cannot. In the first case, when they are collapsed and empty of pneuma, there will be no vacuum to suck the blood across from the venous system, and so no blood will enter the arterial system at all. In the second case, the arteries will behave like a balloon with stiffish walls ("soft reed" to Galen). When such a balloon is inflated and then released, it ejects just what air was blown into it, and no more; the original contents of air remain inside. Thus, if the heart inflates the arterial system with pneuma, and a leak occurs, much pneuma will emerge, but some will always be left; and so long as some remains, no blood will enter the system. Here Galen shows by a remark how little appreciation he had of the maintained force and output of the heart: "We can blow much harder from our mouths into a reed, than the heart could blow into the arteries."

"Let us then", says Galen, "in view of all this, abandon the idea that the arterial system normally contains nothing but pneuma, and agree that it contains at least some blood, as it is always found to do on vivisection, especially if a segment of an artery be tied off and opened up." "If any opponent will not give way to logic as he ought", Galen writes, with typical argumentative abandon, "let us assail him in his own intemperate and illogical language: 'Fire is hot, snow is cold, and you're a fool; therefore it is impossible for only pneuma to be in the arteries.'" As Prendergast remarks, "it must be admitted that Galen never reached that beatitude promised to those who rejoice when reviled and persecuted by men, far less that which is promised to the lovers of peace" [6].

Let us, Galen goes on, shelve the problem of why Nature made two sorts of vessel for one material —blood—and go on to consider how the properties of the arterial system can be accounted for, if it contains both pneuma and blood. Of these, the most obvious is the pulse. And this raised some grave problem for Galen. He does not here make it clear just how he visualized the blood and pneuma together in the arteries; he seems to quiver for a moment on the brink of some idea resembling that of solution of the pneuma in the blood. Had he conceived such an idea clearly, what further progress might he not have made? We have seen already that he was equipped with a belief in what amounted to capillaries, and from other writings [7] we know that he supposed them to exist in the lungs, too, and was thoroughly familiar with the anatomy of the heart valves, although he also deduced the existence of some channels across the interventricular septum of the heart—and is commonly reviled for this last deduction, without receiving his due of credit for the others.

Harvey was armed with a definite idea of solution, and dilates lucidly upon it [8], pointing out how the dissolved "spirits" in the blood cause no physical change, and drawing a comparison between wine, which contains "spirits", and vinegar, which does not, although the volume is the same in each case. But Galen, lacking this idea, fails to make entirely lucid his conception of the pneuma and blood together in the arteries. He mentions that the pulse wave occurs practically simultaneously all the way down an artery, and feels that pneuma itself might travel as fast, but not if blood is present. This notion that the contents of an artery must travel along as fast as the pulse wave is such a natural one that it still requires to be explicitly denied in some textbooks of physiology to-day.

One point is quite clear. Galen felt it manifestly impossible for any pumping of the heart in such a system to cause the pulse wave. Perhaps he imagined the pneuma and blood as entirely separate, like air and water in a part-filled vessel; anyway, he shows no sign of feeling any weakness in his argument, but rather suggests by the brevity of his treatment that any reader would recognize at once the validity of his train of thought.

The other possible cause of the pulse wave is that the arteries actively dilate, through a property of their walls, and in so doing suck in pneuma and blood, not particularly from the heart, but from any part of the system not dilating at the same instant. On this interpretation, to which Galen adheres, the heart serves merely as the originator of the impulse passing along the arteries which causes them to dilate, like the nervous impulses governing the peristaltic contraction of the intestine.

And this active dilation, initiated by a centrifugal impulse from the heart, is the point he sought to demonstrate by specific experiment. His account of the experiment is as follows: "This is what occurs. Free one of the conspicuous and large arteries, first from the skin, and then from the underlying and adjacent structures, so that you can put a ligature round it. Then open it longitudinally and insert a hollow reed or a brass pipe into the artery through the opening, so that it blocks the

wound and prevents hæmorrhage. You will see the whole artery still pulsating, so long as you watch it in this state. But when you put the ligature round, and squeeze the wall of the artery against the reed, you will no longer see the part distal to the reed pulsating, although the transit of blood and pneuma through the lumen of the reed to the ends of the artery is going on as before. If the arteries had this power of pulsating (on their own), even now the part beyond the ligature towards the end would still be pulsating; but it is not doing so. So it is clear that the power is transmitted along the walls; if the power is abolished, the arteries are not moved by the heart. And the views of the Erasistrateans on the movement of the arteries are entirely false. . . . The absence of movement when the ligature has been applied demonstrates clearly that the power that dilates the arteries is transmitted from the heart along the walls of the arteries, and is not the material passing along the lumen." It travels more like the nervous impulse (another "power" to Galen), passing in an instant from the brain to move a muscle. "The speed of the movement agrees with the speed of a 'power', and not with that of matter" [9].

This experiment, which in Galen's hands yielded such an unexpected result had apparently been previously performed by Erasistratus, but with the result we should expect [10]. It was repeated again by William Harvey, in the course of his work upon the circulation. In 1628 he wrote that he had not repeated this particular experiment, anticipating much bleeding, which would confuse observation [11]. However, by 1649 he had changed his mind, possibly to meet some punctilious critic, and gave an account of his performance of it. "For the moment you have thrown your ligature around the artery upon the reed or tube, immediately, by the force of the blood thrown in from above, it is dilated beyond the circle of the tube, by which the flow is impeded, and the shock is broken; so that the artery which is tied only pulsates obscurely, being now cut off from the full force of the blood that flows through it, the shock being reverberated, as it were, from that part of the vessel which is above the ligature; but if the artery below the ligature be now divided, the contrary of what has been maintained will now be apparent, from the spurting of the blood impelled through the tube . . . I can state, after having made the trial, that the inferior part will continue to pulsate if the experiment be properly performed; and whilst they say that when you have undone the ligature, the inferior arteries begin to pulsate again, I maintain that the part below beats less forcibly when the ligature is untied than it did when the thread was still tight. But the effusion of blood from the wound confuses everything, and renders the whole experiment unsatisfactory and nugatory, so that nothing certain can be shown, by reason, as I have said, of hæmorrhage" [12]. It is evident that Harvey's tube fitted very loosely into the artery. He goes on to mention a case he saw himself, where parts of the coat of the aorta were turned to bone, and so presumably could not conduct the impulse onwards, on Galen's hypothesis; yet in this case the impulse did travel past, and down the leg vessels. He regarded this as a natural equivalent of Galen's experiment.

In the present repetition of the experiment, it was hoped to discover, by reconstruction, the reason for the anomalous result obtained by Galen. At the outset, three possibilities suggested themselves. The most attractive was that, by his operation of ligating the artery upon the tube inside, he squeezed the arterial wall, and provoked a spasm of the distal portion of the vessel, thus abolishing its pulsation. The second was that clotting occurred in his tube just at the moment when he applied the ligature—a curious coincidence. And the third, reluctantly considered in view of his extensive experimental experience, was that he was so unobservant as to crush his tube of reed by the ligature without noticing the fact, thus obliterating the arterial lumen, and that he never actually performed the experiment with the brass tube which he also mentions. A fourth possibility will be raised later.

Neither Galen nor Harvey mentioned what animal they chose; however, Galen refers to goats and sheep in a closely similar context elsewhere in his works [13]. For the present experiment, a dog was employed, being the largest animal conveniently obtainable, and anæsthetized with ether, in order to maintain the best possible blood pressure under anæsthesia, and readily palpable pulses. Likewise the artery employed by Galen is not specified, though elsewhere he mentions the femoral [14]. The common carotid was selected, as affording an adequate length without branches. When the neck had been opened, the ether was continued by endotracheal tube.

The right common carotid artery was exposed, and dissected free of the vago-sympathetic trunk and internal jugular vein. The pulse in it was found to be readily palpable, but not visible. The blood flow was controlled by proximal and distal retractors, and the arterial wall was incised longitudinally for a distance just sufficient to allow the insertion of a glass tube about 1 in. long, and of thin wall. The tube was wide enough to fit snugly and slightly to dilate the arterial wall.

The blood loss at this stage was negligible, and the pulse in the distal part of the artery beyond the tube was found to be still clearly palpable and expansile, but of diminished force and volume. A ligature of linen thread, which was probably Galen's material [15], was then applied round the artery at the segment containing the tube, and just proximal to the incision. This produced no change in the pulse in the distal part of the artery; in a further attempt to elicit arterial spasm, a second ligature was applied over the tube just distal to the incision, but without result.

At this point an interval of ten minutes was allowed to elapse, to see whether clotting would occur in the tube, but no change in the distal pulse was found. No anticoagulants had been employed.

At this stage, too, a further possibility was raised, that Galen had inadvertently included the vagus nerve in his ligature, and caused cardiac inhibition by tying it, similar to the well-known inhibition seen on electrical stimulation of the vagus. Galen was fully aware of the course of the vagus nerve (VI cranial nerve in his classification) and of its relation to the carotid artery in the neck [16], of its recurrent laryngeal branch [17], and of the paralysis of the glottis which results from section of the vagus [18]. However, to test the possibility, a femoral cannula was inserted, and the blood pressure recorded by kymograph for the remainder of the experiment. The original ligatures were removed, and the distal pulse again observed, in view of Harvey's observation that this step diminished the pulse; but no change was found, although some slight hæmorrhage from the arterial wall incision followed the removal of the ligatures. Another ligature was then applied as before, but including the right vago-sympathetic trunk. No cardiac inhibition resulted; there was a transient rise in blood pressure, without alteration of pulse-rate or character of distal pulse. Finally, the left vago-sympathetic trunk was also ligated, without including the common carotid, and a repetition of the same transient effects was observed. At the conclusion of the experiment, the distal pulse was observed ninety minutes after the start of the experiment, to find whether evidence of clotting had appeared, but it was still unchanged.

Thus it has not been possible to demonstrate the reason for Galen's observation. No arterial spasm was produced by manœuvres resembling his. No sign of clotting was observed within a reasonable time. The hypothesis that he crushed his tube is only matter for speculation. And in our experiment the result of including the vagus in the ligature was rather that of section of the vagus than of its stimulation.

The effect of ligation of the vagus upon the heart has been frequently tested in the past, in the search for the origin of the heart beat; and Hoff [19] refers to several accounts, the earliest being that of Richard Lower [20]. Hoff regarded these experiments as demonstrating the possibility that ligating the vagus nerve might cause stimulation of the nerve, comparable to electrical stimulation. But it is noteworthy that each experiment he cites in which an effect on the heart is described, consisted in *bilateral* ligation of the vagi; unilateral ligation, in accounts which described it, produced no effect. The effect observed in the bilateral cases consisted admittedly in cardiac irregularities, but also in gross dyspnœa, and always in death of the animal after up to four days. There is no evidence of "vagus escape" as observed with electrical stimulation. Hence it seems quite possible that in all these cases the bilateral ligation of the vagi produced, not a direct inhibition of the heart, but rather choking from bilateral paralysis of the abductors of the larynx. Unilateral paralysis, as is well known, is practically harmless in this respect. In our experiment, choking and dyspnœa were not observed, on account of the presence of the endotracheal tube.

SUMMARY.—An account is given of Galen's views upon the contents of the arterial system, and of a repetition of an experiment done by him, to determine the method by which the arterial pulse is conducted. It has not been possible to account definitely for the anomalous result obtained by Galen, but certain hypotheses are discussed.

ACKNOWLEDGMENTS.—I am indebted to Prof. J. H. Burn, in whose department of Pharmacology at Oxford the experiment was carried out; also to Dr. J. M. Walker, of the department, not only for performing the experiment for me, but also for suggesting the fourth possible interpretation of Galen's result; to Dr. H. M. Sinclair, of Magdalen College, Oxford, for his encouragement and advice, and for access to his invaluable library; and to Dr. Charles Singer for both encouragement and correction.

## REFERENCES

1 WALSH, J. (1929) *Ann. med. Hist.*, **1** (New Series) 378; and (1932) **4**, 126.
2 SINGER, C. (1949) *Proc. R. Soc. Med.*, **42**, 563.
3 Galeni Opera Omnia, ed. Kühn, Leipzig (1821–1833) IV, 703–736. The translations from the Greek are my own, and in the interests of clarity for the present purpose do not always do full justice to Galen's style.
4 ILBERG, J. (1892) *Rhein. Museum Philol.*, **47**, 513.
5 *See* Sir T. Clifford Allbutt's classic, Greek Medicine in Rome, London, 1921—especially chapter 10.
6 PRENDERGAST, J. S. (1928) *Proc. R. Soc. Med.*, **21**, 1839.
7 KÜHN, op. cit., III, 456.
8 HARVEY, W. De Circulatione, in Sydenham Society edition, London, 1847, p. 117.
9 KÜHN, op. cit., IV, 733.
10 —— op. cit., II, 648.
11 HARVEY, W. De Motu Cordis et Sanguinis, in Sydenham Society edition, London, 1847, p. 13.
12 —— De Circulatione, in Sydenham Society edition, London, 1847, p. 111.
13 KÜHN, op. cit., II, 645.
14 —— op. cit., II, 646.
15 MILNE, J. S. (1907) Surgical Instruments in Greek and Roman Times. Oxford, p. 162, and KÜHN, op. cit., II, 647.
16 KÜHN, op. cit., III, 577.
17 —— op. cit., IV, 281, seqq.
18 —— op. cit., II, 841.
19 HOFF, H. E. (1936) *Ann. med. Hist.*, **8** (New Series), 138–144.
20 LOWER, R. De Corde (London, 1669), in R. T. Gunther's Early Science in Oxford, Oxford, 1932, **9**, 86.

# Section of Laryngology

President—C. P. Wilson, C.V.O., F.R.C.S.

[*December* 4, 1953]

Meeting at the Royal College of Surgeons

## DISCUSSION ON THE KERATOSES OF THE LARYNX

**Mr. Munro Black,** Newcastle upon Tyne:

Hyperkeratosis is a change which occurs in squamous epithelium of a physiological or pathological nature commonly as a response to some irritant. When, as in the larynx, the epithelium is normally moist, this change produces the appearance of white plaques and the resultant clinical picture is called leukoplakia. The rather generic term "the keratoses" is useful, but tends to confusion now as limited in meaning to keratosis pharyngis, a condition of different nature and outlook. Accordingly, as far as the larynx is concerned it would seem wise to avoid the term. The same exclusion must apply to the term "pachydermia", which tends to be accepted as referring to a limited thickening of the epithelium in the interarytenoid region.

Hyperkeratosis or leukoplakia of the larynx is a condition of considerable chronicity and tenacity, which is known ultimately to lead in some cases to carcinoma. It ought to declare its presence early by producing dysphonia and thus afford opportunity for study and treatment of a pre-cancerous lesion. Most laryngologists have been humiliated and frustrated by watching such a case "go malignant" whilst under their care.

*Prevention.*—There is no doubt that leukoplakia of the upper respiratory and alimentary tract is becoming less frequent. The general increase in improved oral hygiene, the rarity of a positive Wassermann reaction nowadays and the elimination of septic foci in the sinuses and tonsils must have played a great part in this decrease. Little has been done as yet to improve the situation as regards drinking and smoking, although industrial and professional risks have been publicized and improved. There is a notable age incidence, and this seems to persist.

Apart from all this, there still do occur, although perhaps rarely, cases of leukoplakia in the larynx, and early diagnosis of these is dependent upon adequate examination.

*Diagnosis.*—All cases of dysphonia must be examined early, and there is no excuse for offering treatment without this essential step to diagnosis. Where a diagnosis of chronic laryngitis is made a full clinical and social history is taken, when due consideration must be given to extraneous irritants such as cigarette smoke or industrial vapours, and a full examination made of the whole respiratory tract. I would stress the unreliability of X-ray as a diagnostic measure in sinusitis (as against its essential value with regard to possible lung lesions), and there should be no hesitation in proceeding to antral puncture. Also a Wassermann reaction and blood count will be necessary.

The finding and elimination of any extrinsic or intrinsic irritants will allow the recovery of many such cases.

There will be a residuum of cases in which the changes in the larynx persist and for which no cause can be found.

They tend to occur in middle or later life, so that the sex hormones may play some part, especially as this lesion is more common in the male and we know that the larynx can be markedly altered by such hormones. Also, hyperkeratosis is a known dermatological disturbance associated with the menopause, and, of course, common in old people. I have gained a general impression in my cases of thick-set, red-skinned people.

Examination locally reveals a dryness and redness of the pharyngeal and laryngeal mucosa—at times so red as to suggest petechial hæmorrhages. The white plaques occur mainly on the vocal cords, but there is great variation both in occurrence and distribution. Later in its progress there may be marked thickening of the mucosa with perhaps ulceration suggestive or conclusive of carcinoma.

It is at this stage—early in the case history—that I have had some encouragement from the use of vitamin A, giving about 100,000 units per day. It is difficult, however, to assess results owing to the known natural course of the condition.

Failing a definite improvement under treatment, the diagnosis must be doubted and recourse made to biopsy if there is any tendency to productivity or ulceration in the lesion. The necessary anæsthesia offers also an opportunity for thorough and intimate examination of the larynx by endoscopy and careful selection of the material for biopsy. Diagnosis may be at once surprisingly established that carcinoma is already present, but often a less definite answer is given. I would, however, stress the importance of the clinical opinion as well, because at this stage of doubt and danger it would seem that something must be done.

*Treatment.*—This change in the larynx is a general and not a localized lesion. Ultimately I believe it will be prevented or treated by general measures, but until then treatment should lie between general irradiation of the larynx or its total removal by operation. As long as the lesion has not proceeded to much scarring and loss of blood supply to the mucosa and is in a productive stage, I would advise irradiation. I would justify primary laryngectomy only in the case of very long history in which œdema and scarring of the mucosa are present.

This, then, has been my approach to the management of these cases of hyperkeratosis of the larynx, and is illustrated now by case histories.

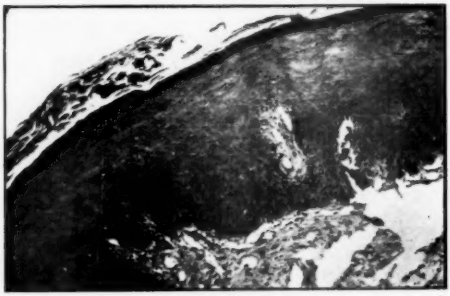


FIG. 1 (*Case* 1).—Section of vocal cord showing thick epithelium with para - and hyper-keratosis.

I am not including any cases which, although having the clinical appearance of leukoplakia, recovered rapidly to normal after correction of extrinsic or intrinsic factors of irritation. There were also others which recovered I think with the aid of vitamin A, leaving the following cases:

*Case* 1 (Fig. 1).—F., aged 38 when first seen in October 1946 with dysphonia. Nothing was found and the condition recovered. She returned in February 1951, when the vocal cords were thick and red, and showed on biopsy "grossly thickened squamous epithelium with thin parakeratotic superficial layer".

In September 1951 the larynx was unchanged, but there was troublesome nasal vestibulitis and a general redness of the skin. Her general appearance suggested possible hypothyroidism, but this was negated. A marked general upper inflammatory infection occurred in May 1952, when leukoplakia was most evident in the larynx. Vitamin A produced or coincided with a real improvement. In July 1953 there was a slight relapse, but by September her larynx seemed about normal again. Recently she has had sublingual ovarian hormone with evident general improvement.

*Case* 2 (Figs. 2 and 3).—M., aged 40 when first seen in November 1950 with recent dysphonia. He had had similar previous trouble a year before during harvest collecting. There was a white proliferative leukoplakia of the anterior halves of both vocal cords, reported on biopsy as "hyper- and para-keratosis". Nothing was found on general investigation. The condition has varied since then, and vitamin A has not helped. It is bad at the moment, and further biopsy will be arranged. He may be a case for irradiation.

*Case* 3 (Figs. 4 and 5).—M., aged 34 when first seen in January 1952. Two years previously he had had dysphonia for about three months, and again about six months ago. Full investigation elsewhere had not revealed any cause for this. The larynx was dry and red with leukoplakia mainly at the posterior parts of the vocal cords. Biopsy was reported as "thickened squamous epithelium with parakeratosis, marked chronic subepithelial inflammation". He was a thick-set, red-skinned man who had had trouble with "dermatitis". In February 1952 he was given an ACTH drip, but there was no response generally or locally. He was given vitamin A and improved. In June 1953 the larynx looked about normal, but he had developed a nodule and an almost contact ulcer posteriorly. After a recent acute attack of tonsillitis the tonsils have been removed. Opportunity was taken for another biopsy of the larynx.

These three cases are still under consideration and will be used for further study, especially of the effect of sex hormones.

The next group is of those treated by irradiation. It has been stated on several occasions that irradiation can play no part in the treatment of leukoplakia, but I feel that this opinion has been

FIG. 2 (*Case* 2).—Section of vocal cord showing hyper- and parakeratosis.

FIG. 3 (*Case* 2).—Recent biopsy showing parakeratosis.

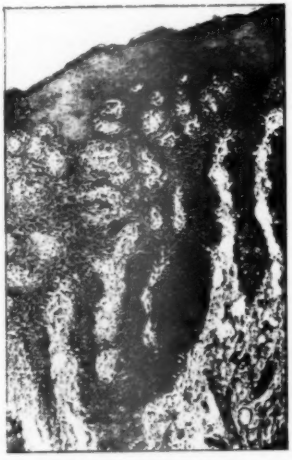


FIG. 4 (*Case* 3).—Section of vocal cord showing thick epithelium with parakeratosis.

FIG. 5 (*Case* 3).—Present biopsy showing parakeratosis.

based on experience with advanced cases, especially of the tongue with fibrosis and vascular thrombosis. If hyperkeratosis is treated by irradiation before such interference with the blood supply to the epithelium it should react well.

In the following cases in which irradiation has been by deep X-ray, treatment has been given through two or three fields extending over at least thirty days, and giving between 4,000 r and 5,000 r with a half value layer of 3 mm. Cu.

*Case* 4 (Fig. 6).—M., aged 52 when first seen in July 1950. He had had dysphonia for about one year and showed a thick leukoplakia of the whole length of both vocal cords. General examination did not reveal any cause. Biopsy was reported as "almost a keratinizing squamous-cell carcinoma". The larynx was treated by X-irradiation, and has remained normal since then.

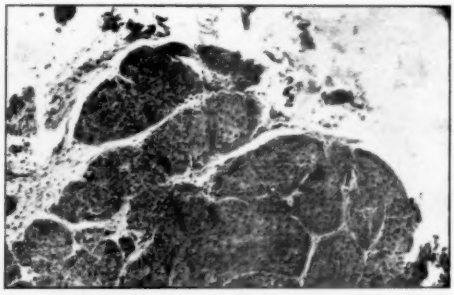


FIG. 6 (*Case* 4).—Larynx biopsy suggestive almost of carcinoma.

*Case* 5 (Fig. 7).—M., aged 79 when first seen in October 1952, with six months dysphonia. The larynx showed a thick leukoplakia of the whole right vocal cord and of the posterior half of the left vocal cord. General examination did not reveal anything of note, and biopsy was reported as "keratosis laryngis with marked hyper- and para-keratosis, very like carcinoma". The larynx was treated by X-irradiation, rapidly returned to normal, and has remained so since.

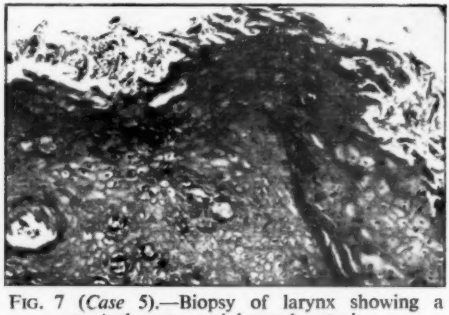


FIG. 7 (*Case* 5).—Biopsy of larynx showing a marked para- and hyper-keratosis.

*Case* 6 (Fig. 8).—M., aged 56 when first seen in July 1951 with eight months' dysphonia. The larynx showed a limited leukoplakia of the right vocal cord. General examination did not reveal anything of note, and biopsy was reported as "hyperkeratosis", and on repeat as "epithelial papillosis, perhaps malignant". The lesion was treated with local radium by the Finzi-Harmer method, using seven 1 mg. needles and one 2 mg. needle *in situ* for six days. It has remained well since.

FIG. 8 (*Case* 6).—Biopsy of larynx showing marked hyperkeratosis.

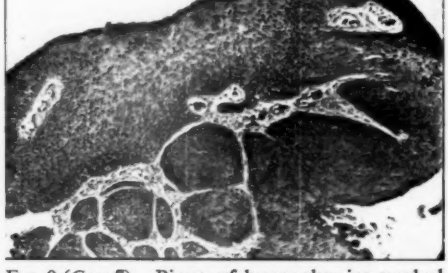


FIG. 9 (*Case* 7).—Biopsy of larynx showing marked changes in epithelium, accepted as carcinoma.

The final cases have required laryngectomy:

*Case* 7 (Fig. 9).—F., aged 39 when first seen in September 1950, with about eight years' dysphonia. The larynx showed ulceration and fixation of the right side, and an ulcerated but mobile left vocal cord. Biopsy was reported as "safer to accept as carcinoma". This lesion was considered unsuitable for X-irradiation and laryngectomy was advised but refused. Accordingly, X-irradiation was given but failed, and a further biopsy six months later showed definite carcinoma. Laryngectomy was performed in June 1951, and all is well to date.

← FIG. 10 (*Case* 8).—Larynx removed at operation, showing extensive carcinoma, but also greater extent of epithelial proliferation, marked mucosal thickening and scarring.

FIG. 11 (*Case* 8).—Section of epithelium distant from the evident carcinoma, showing marked parakeratosis.

FIG. 12 (*Case* 8).—Section through a nodule of thickened epithelium even more distant from the evident carcinoma.

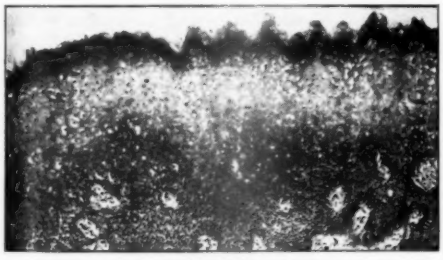


FIG. 11.

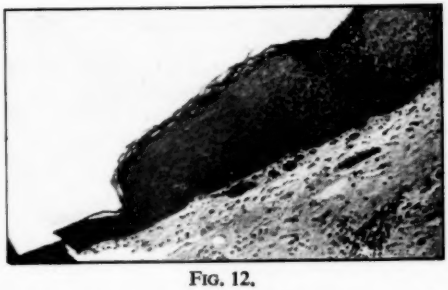


FIG. 12.

*Case* 8 (Figs. 10, 11 and 12).—M., aged 54 when first seen in February 1952 with about five years' dysphonia. About nine months previously he had been investigated elsewhere and a biopsy reported as "hyperkeratosis", more recently a repeat was accepted as "very like carcinoma". The larynx showed marked general scarring and ulceration, with fixation mainly on the left side. Biopsy was reported as "carcinoma". Laryngectomy was performed in February 1952, and he has remained well to date.

**Dr. B. T. Davis:** Department of Pathology, University of Birmingham:

*The Pathology of the Keratoses of the Larynx*

There is no keratinization of the epithelium in the healthy larynx, which is lined with stratified squamous epithelium on the anterior surface of the epiglottis, on the upper part of the posterior surface of the epiglottis, on the aryepiglottic folds, and over the vocal cords. The remainder is lined with ciliated columnar epithelium which is usually pseudostratified. Keratinization can occur as a result of overstimulation or irritation of the squamous epidermal cells by any persistent inflammatory or neoplastic process. It can occur in those parts of the larynx normally lined with ciliated columnar epithelium only after metaplasia into squamous epithelium has taken place.

The term hyperkeratosis is defined by Macleod and Muende (1946) as "hypertrophy of the stratum corneum in which it is thickened by an increase in the number of its component horn cells". There is no stratum corneum in the larynx until keratinization has occurred, so that for practical purposes keratosis and hyperkeratosis in the larynx are synonymous terms, though hyperkeratosis rather implies a thicker layer of horn cells than is seen in simple keratosis.

The only reliable way of distinguishing and classifying diseases is based upon their ætiology, and the confusion in terminology of laryngeal conditions associated with keratosis implies that the ætiology and pathology of many laryngeal diseases is still not well understood. Most of these lesions are uncommon and some are very rare. Biopsy specimens from the vocal cords are of necessity small, and are often superficial so that histological investigation is difficult, often unrewarding, and may be misleading. Post-mortem specimens are rarely available and usually show late stages often complicated with ulceration, infection or neoplastic change. The study of the pathology of the larynx, together with most lesions seen in the ear, nose or throat, has tended to be neglected by pathologists.

Many widely varying and often contradictory opinions have been expressed regarding the ætiology of laryngeal keratoses, but so far as I have been able to discover, adequate controlled statistical information on this aspect is not available.

There is a group of chronic inflammatory lesions of the larynx which are often associated with keratosis.

*Chronic hyperplastic laryngitis* is usually a diffuse condition but may be localized. It may follow repeated attacks of acute laryngitis but usually only in cases complicated by chronic upper respiratory or dental infection, "vocal abuse", exposure to dusty or irritant atmospheres, or over-indulgence in smoking or alcohol, especially spirits.

Histologically there is hyperplasia of the mucous membrane sometimes with metaplasia of the columnar epithelium into squamous epithelium. Keratosis is frequently, but not always, present. The lamina propria shows hyperæmia, heavy cellular infiltration of chronic inflammatory type, fibrosis, and hypertrophy of the mucous glands. Those cases in which vocal abuse is a prominent ætiological factor may show changes most marked in and about the vocal cords.

*Pachydermia of the larynx* is a name best confined to the condition described by Virchow (quoted by Jackson and Jackson, 1946) which is a symmetrical indurated hypertrophic condition involving the posterior ends of the vocal cords and the tissue in the posterior commissure and which is extremely rare. It is probably a variant of chronic hypertrophic laryngitis. The original cases were from men who regularly indulged in nocturnal carousing. Chronic alcoholism, shouting and singing out of doors, and possibly heavy smoking, appear to be the important ætiological factors.

Histologically there is thickened, usually keratotic, epithelium which is not ulcerated and which shows irregular dendritic downward processes into the thickened, fibrotic chronically inflamed lamina propria. There is no breach in the basal layer of the Malpighian layer. The condition must be distinguished from contact ulcer of the larynx described by Chevalier Jackson (1928) where there is ulceration and no pachydermia or keratosis.

*Singers' nodules* (chorditis nodosa), *fibroma*, and organizing *hæmatoma* of the vocal cords are lesions often covered with keratotic epithelium.

The lesions so far described are benign and do not show any tendency to malignant change.

Three varieties of laryngeal papillomata are described:

(1) *Multiple papillomata* characteristically seen in children and possibly due to virus infection. These do not show keratosis or malignant change except in very rare cases.

(2) *Simple solitary papilloma* without keratinization or tendency to malignant change.

(3) *Keratinizing* or *hyperkeratotic papilloma.*

The last is the commonest variety of laryngeal papilloma according to Eggston and Wolff (1947) who reported 398 cases of this type out of 664 cases of all varieties of laryngeal papilloma. The lesion consists of an area of papilliferous hyperplastic epithelium with overlying keratosis and usually a fairly smooth surface. It should be considered as a localized variant of leukoplakia and is often spoken of as leukoplakia of the cords. This would appear to be the condition from which the Emperor Frederick III of Germany suffered when Crown Prince and which ultimately became a frank carcinoma.

*Leukoplakia and the so-called keratosis of the larynx* are manifestations of a single disorder. Keratosis of the larynx should not be confused with the totally different condition keratosis pharyngis, and consists of a localized well-circumscribed patch or patches of hyperplastic squamous epithelium with an overlying mass of cornification usually occurring on the anterior or middle thirds of the vocal cord. The keratinous tissue sometimes has a papilliferous, spiky appearance. There should be no breach in the basal layer of epithelium and only slight fibrosis or inflammatory infiltration of the lamina propria. This must be a very rare condition, and a superficial biopsy of a localized keratinizing squamous-celled carcinoma would have a similar appearance to that from a superficial biopsy of keratosis of the larynx.

One wonders how many cases thought to be keratosis of the larynx are, in fact, cases of either intra-epithelial carcinoma or even invasive carcinoma. Some published cases did in fact have underlying carcinoma, for example the case of Gordon (1950). In any case there appears to be no doubt that the condition is precancerous and requires careful treatment and observation. The only histological difference between these cases and hyperkeratotic papilloma is that the latter condition shows a papilliferous heaping up of the prickle-cell layer.

Leukoplakia of the larynx is the name which should be applied to a more widespread lesion in the larynx of a similar process. It is in most ways comparable with leukoplakia occurring elsewhere in the body, and similarly is undoubtedly precancerous.

Histologically there is a hyperplasia of the squamous epithelium with marked keratosis. The basement membrane is intact, but there are often small irregular projections into the lamina propria which shows a rather scanty, diffuse infiltration with chronic inflammatory cells. There are usually numbers of thin-walled vessels and some degree of œdema. In the later stages there is fibrosis. Mucous glands may show cystic dilatation due to obstruction of their ducts by the horny tissue.

The ætiology of this group of conditions remains unsettled but Clerf (1946) gives the following suggested causes:

Excessive smoking, especially of cigarettes.

Chronic laryngitis.

Vitamin deficiency, especially disturbances of vitamin-A metabolism. Graham (1942) describes a case in which extra vitamins A, B, C and D were given, following which there was considerable retrogression of keratosis with disappearance of the generalized hyperæmia, and the patches did not recur following surgical removal as they had done previously.

Clerf did not consider that excessive use of the voice or alcoholism were important factors, but Jackson and Jackson (1942) appear to consider that they are, and, in any case, excessive use of the voice and alcoholism are often factors in the causation of chronic laryngitis. Clerf also states that the incidence of syphilis did not appear greater among patients with keratosis.

There is no need to describe the pathology of ordinary keratinizing squamous carcinoma of the larynx but I think that intra-epithelial carcinoma should be mentioned. According to Altmann, Ginsberg and Stout (1952) this condition is not very rare. They collected 29 cases out of 312 laryngeal cancers, with 19 further cases associated with invasive carcinoma.

The duration of symptoms (weeks or a few months), sex incidence (10 males to 1 female), and age (over 40 years) of the patients are similar to those found in invasive carcinoma. The lesion is commonest on the anterior third of the vocal cord and may spread to the opposite cord.

Not infrequently the carcinomatous epithelium shows a tendency to keratinization and may become papillary. The histological appearances may be rather similar to those of keratinizing papilloma or keratosis of the larynx. There is neoplastic overgrowth of the stratum Malpighii with pleomorphic cells showing gross disorientation. These cells are often spindle shaped. The cell nuclei vary considerably in size and shape, and multinucleate forms may be found. The stratum germinativum cannot be distinguished from the rest of the stratum Malpighii, but the basement membrane remains intact and there is no invasion of the subepithelial tissues.

*Conclusion.*—Lesions in the larynx which show keratosis, which are not obviously inflammatory and do not respond adequately to treatment, should be treated with great suspicion as being premalignant or malignant.

## REFERENCES


ALTMANN, F., GINSBERG, I., and STOUT, A. P. (1952) *Arch. Otolaryng., Chicago*, **56**, 121.

CLERF, L. H. (1946) *J. Amer. med. Ass.*, **132**, 823.

EGGSTON, A. A., and WOLFF, D. (1947) Histopathology of the Ear, Nose and Throat. Baltimore.

GORDON, G. R. (1950) *Laryngoscope, St. Louis*, **60**, 1201.

GRAHAM, H. B. (1942) *Arch. Otolaryng., Chicago*, **36**, 735.

JACKSON, C. (1928) *Ann. Otol. Rhin. Laryng.*, **37**, 227.

——, and JACKSON, C. L. (1942) Diseases and Injuries of the Larynx. New York.

——, —— (1946) Diseases of the Nose, Throat and Ear. Philadelphia and London.

MACLEOD, J. M. H., and MUENDE, I. (1946) Pathology of the Skin. London.


**Mr. W. H. Bond**, Queen Elizabeth Hospital, Edgbaston, Birmingham:

*Radiotherapy of Hyperkeratosis*

The radiotherapist has no interest in the management of the benign hyperkeratoses of the larynx, but has a part to play in the treatment of the two remaining groups, namely the localized laryngeal keratosis and leukoplakia of the cords. The former tumour is met in the cancer-bearing age, appears at a site on the cord where invasive tumours are commonly seen, and in the light of modern views on intra-epithelial tumours can be logically regarded as a well-differentiated squamous-cell carcinoma of intra-epithelial type. This tumour should respond to radiotherapy, and in review of 106 intrinsic carcinomata seen in the United Birmingham Hospitals between 1936 and 1947, five laryngeal keratoses were found, three being successfully treated by irradiation, one case requiring laryngectomy in the sixth year for a tumour of the opposite cord.

In leukoplakia of the cords with or without changes in the vestibule and false cords, surgery is necessarily extensive, and it is in this class of case where radiotherapy, if successful, has so much to offer. In deciding on the place of radiotherapy in their management, apart from the well-known risks of irradiation damage it is known that the response of the premalignant lesion is inconstant.

Glücksman (1950) found that 30% of the recurrences of oral and faucial cancer after successful radiation treatment of the primary tumour were due to persistence of premalignant lesions. That these may be converted to true malignancy by doses of irradiation barely sufficient to induce a mucosal reaction was suggested by Mottram (1937), who showed that relatively low doses of irradiation would act as a co-carcinogen and increase the number of tumours appearing on rabbit's skin prepared with benzpyrene. The incidence of malignant tumours was, however, reduced when the dose was much higher (Cramer, 1932).

These considerations imply that in planning any treatment scheme, prophylactic, moderate or modified irradiation has no place and if irradiation is undertaken the final dose level achieved must be high and associated with the full reactions seen with whatever technique a particular radiotherapist uses in dealing with frank malignancy. In Fig. 1 the first curve shows the percentage of oral and pharyngeal cases developing mucosal reactions to any total dose delivered over a period of three weeks. The second curve, from a series of oral and faucial carcinomata treated by radium beam, shows the percentage of cases regressing for at least a year after treatment to various dose levels in the same period of time. The similarity of these two curves prompted the drawing of the third which I believe relates the incidence of damage in normal tissues to larger doses given in the same three-week period. From these curves it should be noted how few tumours may be expected to

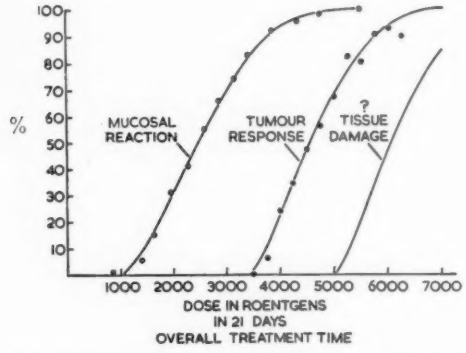



FIG. 1.—Relationship of mucosal reaction, tumour regression and tissue damage to tumour dosage in three weeks' treatment.

regress if mucosal reactions do not appear in the great majority of cases; below a certain level few if any tumours will respond, though within a fairly short range of dose the risk of damage increases alarmingly. There is little doubt that similar dose-response curves apply to the larynx and for these reasons full therapeutic dosage is called for. Because of the high dose required, small beam-directed fields must be used restricted to the area involved, and a technique, preferably by radium beam, must be selected such that skin reactions are minimal, remembering that surgery is inevitable in a proportion of these cases.

In selection of cases for radiotherapy one's experience with oral leukoplakia is invaluable. Slow regression of the localized patch follows high dosage irradiation; on the other hand the prompt regression of the diffuse leukoplakias of the mouth is poorly maintained, possibly because of the necessarily lower total dose given to the wide area involved. In the larynx primary consideration should be given to the extent of the change. The most suitable cases for radiotherapy are those where the disease is confined to the cords, without fixity of tissues and with a satisfactory local blood supply. The area to be treated should be small so that a satisfactory dose can be given without difficulty, the total dose being adjusted by the severity of the mucosal reaction. I do not think radiation should be given where there is diffuse leukoplakia, nor where there is scarring or other chronic inflammatory change, since apart from the difficulty of treating the bigger volume adequately, should infiltrating tumour appear subsequently, no case is more difficult to deal with than the carcinoma spreading through heavily irradiated tissues. The extensive area involved is but an index of the epithelial instability and such cases are best dealt with by surgery or watched into malignancy.

## REFERENCES

CRAMER, W. (1932) *Brit. J. Radiol.*, **5**, 618.

GLÜCKSMAN, A. (1950) *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 267.

MOTTRAM, J. C. (1937) *Amer. J. Cancer*, **30**, 746.

Mr. **R. Thomas** reported a family where the grandfather, father and son suffered from keratosis laryngis. The grandfather died in old age of another disease; the father had been observed for twenty-eight years—his larynx was gradually returning to normal at age 73; the son, aged 46, had been observed for seven years. Was it possible that a familial type of keratosis was unlikely to become malignant? He would be glad to hear if any member of the Section had noted a familial tendency.

He had notes of 5 other cases. One had become malignant and died of recurrence following laryngectomy. Serial sections of the vocal cord removed at laryngofissure from the next case showed no malignant changes; this patient remained well. 2 recent cases had radiotherapy; the keratosis disappeared within a month of treatment. Another case was waiting for radiotherapy.

He suggested that, if, according to previous speakers, keratosis laryngis responded to radiotherapy, it would be kinder to refer patients—at least those with lesions restricted to one cord—to the radiotherapist straight away rather than to ask them to come up every three months for observation, with the ever-present fear in the minds of both patient and surgeon that the disease might suddenly become malignant and untreatable.

**Professor Victor Lambert** thought that everybody agreed that hyperkeratosis was a premalignant condition, but that its ætiology had never been determined. It was virtually impossible to decide when its premalignant condition became frankly malignant. In this state of ignorance he thought that it was the duty of the laryngologist to protect the patient from the risk of malignancy by early treatment, preferably by irradiation. He believed that this applied when the hyperkeratosis was diffuse and not localized, and particularly when it attacked the posterior ends of the cords, because it was from the posterior end that metastases and malignancy were most common.

He was interested in Mr. Thomas's description of the familial hyperkeratosis. He, himself, had seen three members of a family develop pyriform fossa malignancy superimposed upon some hypopharyngitis.

It was inevitable that some of these cases might be treated at the wrong time, but it was better to treat them too early than too late.

**Mr. W. I. Daggett** said there was one type of keratosis which he gathered that Mr. Black had dismissed as being allied to keratosis pharyngis and therefore unimportant.

This was a type in which white keratotic masses like a starfish presented between the cords attached to their free margins more on one side than the other. They could not be compared with the tiny spikes upon the tonsil seen in keratosis pharyngis: surely this condition was a manifestation of true keratosis of the larynx? Such masses were not very difficult to strip off and were reported upon by the pathologist as not malignant.

He had seen 3 such cases, one in which the cords had been stripped on three occasions: eventually he performed a laryngofissure and excised the worse affected cord. The patient remained well for eighteen months and then the larynx presented obvious signs of carcinoma and had to be removed. In another case laryngofissure was performed and a cord excised, a beautiful false cord of fibrous tissue formed but later new spikes could be seen on the free border. This patient died of coronary thrombosis a year later. The third patient submitted to laryngofissure, again a smooth false cord formed and later small spikes appeared on the free edge: three years later the spikes had disappeared. Had Mr. Black recognized such cases?

**Mr. Munro Black** said that when he objected to the word keratosis, it was essentially a matter of nomenclature. The term had become associated with a separate entity (keratosis pharyngis), which was of a quite different nature, and the characteristic lesion of which could occur in the laryngeal mucosa. It was an attempt to be sure that they all meant the same thing when they used the same term.

**Mr. F. C. W. Capps** agreed that these cases should be treated by radiotherapy. He would utter one warning from experience in treating these cases, which was that they should not only be treated by what was thought to be a good dose, but what was clinically a good dose. He remembered the case of a woman of 52 who had white vocal cords who was treated with 4,000 r in four weeks. It all disappeared and it was thought it would go no further. She returned within six weeks with a recurrence and was given another 2,700 r. People varied a good deal in their tolerance of radiotherapy: what was a huge dose at 2,000 r for some people was very little to somebody else who could stand up to 6,000 or 7,000 r. A second case was given 5,000 r and there was a terrific reaction. He was sure that it was to the limit of clinical tolerance that treatment should be given.

**Mr. W. H. Bond** agreed with what had been said but the laryngologist and radiotherapist must work together. They must watch the patient and have a clear idea of what they were aiming at. Dosage must be high, 5,000 or 6,000 r could be given in four or five weeks but the total dose depended on how much was given each day, even weekend treatment made a great deal of difference.

**Mr. R. D. Owen** asked what Mr. Munro Black meant when he showed his last slide of the infiltration of the larynx (Fig. 10) and said "That is what must be avoided". Did he mean that leukoplakia was a

reversible lesion and could be treated conservatively? Secondly, when he mentioned performing a Finzi-Harmer on one side, if he found a recurrence of leukoplakia on the other side later on, would his treatment for that be further irradiation or extirpation of the larynx?

**Mr. Munro Black** replied that he thought leukoplakia was a reversible lesion, again realizing that it was a clinical picture, not a pathological term. The picture of leukoplakia when followed over a considerable period of time would vary considerably, and could in fact disappear and return again. What was now hoped was that in the first place we ought to be able to prevent leukoplakia, knowing how it is caused and, further, when diagnosed it ought to be possible to treat it and cure it. The last case presented was a most advanced condition, and a most disappointing state of affairs that such a case came to treatment only so late in its course.

He was not in favour of the Finzi-Harmer treatment for the condition discussed. If a patient had a Finzi-Harmer on one side, it would mean that a fairly large dose of irradiation was given also to the opposite vocal cord. especially at its anterior end. Another Finzi-Harmer on that opposite side would be dangerous.

**Professor Victor Lambert** said that the only bilateral Finzi-Harmer operations he had done were carried out for malignancy starting as hyperkeratosis. He did not consider Mr. Daggett's description as that of hyperkeratosis: he did not know quite what to call it, but it was not his conception of a hyperkeratotic state.

**Dr. B. T. Davis** said that intra-epithelial carcinoma was a condition in which there was no break in the basal layer but the cells did show carcinomatous characteristics. They had lost their normal character. Quite frequently they became spindle-shaped, frequently of varying size and shape, there were frequently large vacuolated cells and occasionally one saw multinuclear cells. Bowen, who first described the condition, laid emphasis on these characteristics of the cells which were malignant.

**Mr. Munro Black** wished to draw attention to an apparent sealing effect of irradiation, that although a carcinoma in the larynx might not be cured by irradiation, this did seem to limit spread. He mentioned one case in which a larynx was removed five years after irradiation, and he was sure that growth had remained there all that time without spreading. As a final word, he did wish to stress the question of ætiology, and why marked prolonged irritation to a larynx in some cases produced these lesions under discussion, while in others there was no harmful effect at all.

# Clinical Section

President—JAMES L. LIVINGSTONE, M.D., F.R.C.P.

[*December* 11, 1953]

**Spontaneous Hæmopneumothorax.**—F. M. MCGOWN, M.D., M.R.C.P. (for R. D. GREEN, M.D., M.R.C.P.).

*History.*—Mr. R. B., aged 23, shop assistant, on 20.8.53 ran up a hill pushing a pram; he suffered no immediate ill-effects but about four hours later, when sitting down, felt a sudden severe pain in his left lower chest; this passed off after several hours. He had no further symptoms until sixteen days later when the pain recurred together with a slight dry cough. He became collapsed and dyspnœic, and was admitted to Paddington General Hospital on the following day. There was no past or family history of chest disease.

*Examination.*—On admission to hospital on 6.9.53 he was gravely ill with pale, cold extremities, and severe dyspnœa. T. 96·8° F., P. 154, R. 40. No marked pallor of conjunctivæ. C.V.S.—B.P. 110/70. Heart sounds best heard near sternum. R.S.—Trachea to right. Impaired percussion note and absent breath sounds at left base. Abdomen and C.N.S. normal. Chest X-ray (6.9.53): Large left hydropneumothorax with a fluid level at the 7th rib posteriorly. Mediastinum displaced to right.

*Progress and treatment.*—He improved slightly with rest and following aspiration of two pints of blood from the left pleural cavity. During the next three days the bleeding continued, and he collapsed suddenly twice, and more gradually once, recovering after transfusions. On 8.9.53 after receiving 7 pints of blood, his hæmoglobin was 29%, and his condition was very poor. Thereafter he improved slowly but steadily. In all 12 pints of blood were transfused in the first four days, and 14 pints of blood-stained fluid were aspirated from his pleural cavity in the first six days. There was no further evidence of bleeding, and aspirations became difficult. Owing to the risk of further hæmorrhage, intrapleural injection of streptokinase and streptodornase was not started until 8.10.53. It produced a severe general reaction, and the patient refused further injections. He ran a variable fever until 16.10.53, which then subsided. Antibiotics and a further 3 pints of blood were given during this period. He was discharged to convalesce on 20.10.53.

Serial X-rays of the chest showed a gradual return of the mediastinum to the centre, loculation followed by reabsorption of the air and fluid in the pleural cavity, and partial re-expansion of the lung, but on 8.12.53 an opaque border up to 1½ in. wide persisted around the lung. No cause for the hæmopneumothorax was apparent. On 16.12.53 the patient remained dyspnœic after one flight of stairs, had a mildly productive morning cough and poor chest expansion on the left, but was improving slowly following breathing exercises.

*Comment.*—Up to July 1953, 93 cases of spontaneous hæmopneumothorax had been described with 19 deaths (Borrie, 1953). The ætiology is similar to that of spontaneous pneumothorax. Necropsy reports (Helwig and Schmidt, 1947) and findings at operation reveal ruptured emphysematous bullæ with bleeding either from the site of the rupture or from pleural adhesions. Experience with massive hæmorrhage complicating artificial pneumothorax therapy shows that the bleeding is often from a large vessel in an adhesion attached to the chest wall, and that the part of the adhesion attached to the lung usually contracts and does not bleed.

The rarity of massive hæmorrhage in spontaneous pneumothorax and confusing clinical signs may make initial diagnosis difficult until a radiograph has been obtained. Treatment is usually by transfusion and pleural aspiration, but since 1950 thoracotomy has occasionally been performed during the early stages, both to arrest the hæmorrhage and also to cut short the illness by the removal of blood and fibrin from the pleural cavity (Beatty and Frelick, 1952; Borrie, 1953).

Operation was seriously considered in the present case, but the risks of conservative treatment appeared less than those of an emergency thoracotomy, and the bleeding did, in fact, cease spontaneously. The patient, however, remains with incomplete expansion of his lung and although this is improving, decortication may yet be necessary.

We are grateful to Mr. T. Holmes Sellors for advice on the management of the case, and to Dr. M. Porter for assistance with the treatment.

POSTSCRIPT (19.3.54).—Following breathing exercises, the lung expanded further, but still incompletely. On 1.2.54 decortication of the left upper lobe was performed by Mr. Holmes Sellors at Harefield Hospital A fibrous membrane was found covering almost the whole upper lobe and containing organizing blood clot The underlying lung was healthy and there was no evidence of tuberculosis on microscopic examination of the tissue removed. The post-operative course and final X-ray were satisfactory.

## REFERENCES

BEATTY, G. A., and FRELICK, R. W. (1952) *Ann. intern. Med.*, **36**, 845.
BORRIE, J. (1953) *Brit. med. J.*, ii, 16.
HELWIG, F. C., and SCHMIDT, E. C. H. (1947) *Ann. intern. Med.*, **26**, 608.

**Arteriovenous Aneurysm of the Neck.**—L. T. COTTON, B.M., F.R.C.S. (for H. C. EDWARDS, C.B.E., M.S., F.R.C.S.).

Mrs. E. G., aged 60, admitted under the care of Dr. Terence East. In June 1944 she sustained multiple injuries in a flying bomb explosion, and was wounded in the right side of the neck and right arm. A pulsating hæmatoma of the neck causing dysphagia and a bruit was noted. In August 1944 she was evacuated to Glasgow when the aneurysm was explored by Mr. J. Dunbar. Before operation a complete abductor palsy of the right vocal cord was found.

On August 16, 1944, an arteriovenous aneurysm of the right common carotid artery and internal jugular vein was explored. Two communicating veins were tied and ligatures were placed above and below the aneurysm. The internal jugular vein was sutured. A thrill was present in the region of the operation scar some days after.

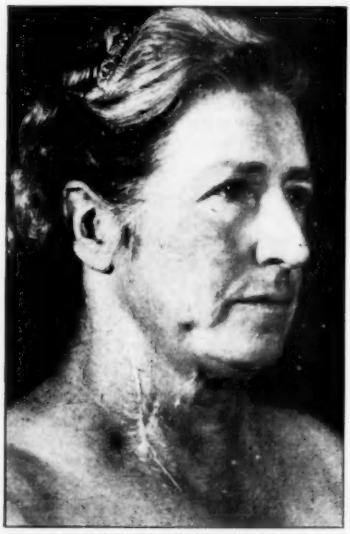


FIG. 1.—Photograph showing operation scar.

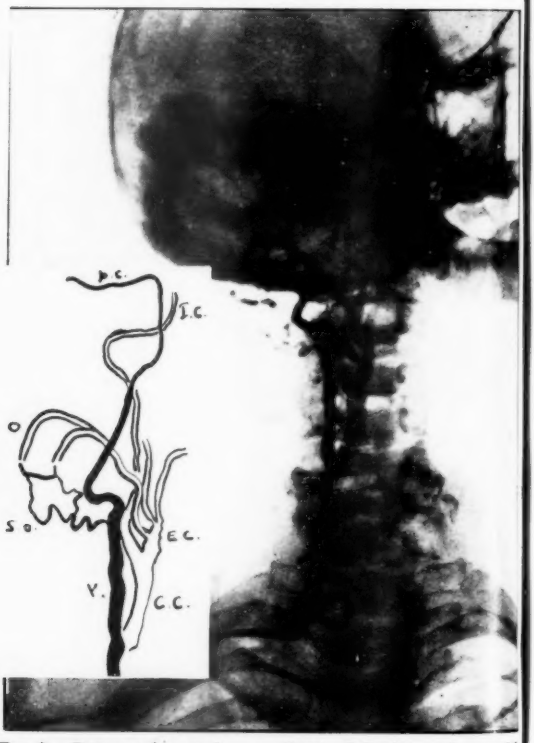



FIG. 2.—Retrograde arteriogram. Inset—I.C., internal carotid; E.C., external carotid; C.C., common carotid; v., vertebral; s.o., suboccipital; o., occipital; p.c., posterior cerebral.

She was admitted to King's College Hospital on October 7, 1953, complaining of dyspnœa on exertion for two months before admission. She was also suffering from paroxysmal dyspnœa at night, retrosternal discomfort on exertion, swelling of the ankles, lassitude, and a constant noise in the head and neck.

On examination her appearance was myxœdematous. The neck showed the scars of her injury and operation on the right side (Fig. 1) with increased pulsation beneath them. There was a continuous thrill to be felt maximal over the upper part of the right common carotid artery, with a very loud to and fro murmur to be heard on auscultation. Attempts to obliterate the murmur by pressure failed as the neck was tender. There was no obvious venous pulsation. The pulses and blood pressures in both arms were identical. Blood pressure 140/80 mm.Hg. On admission there were signs of early congestive failure which disappeared in bed with diuretics, digitalis, and thyroid extract, given very cautiously.

*Investigations.*—Chest X-ray showed a generalized cardiac enlargement and pulmonary congestion. Venous pressure normal. Hæmoglobin 98%. White blood cells 7,400 per c.mm. Plasma cholesterol before therapy 390 mg.%, after therapy 328 mg.%. Basal metabolic rate minus 13%. Radio-active iodine uptake, thigh-neck clearance 1·9 (on the low side of normal).

Laryngoscopy showed persistence of the palsy of the right recurrent nerve. X-rays of the neck revealed no bony abnormality nor any foreign body. A retrograde angiogram was performed via the right brachial artery (Fig. 2). The site of the fistula was not shown. It appeared that the common carotid artery had been tied well below its bifurcation and that filling of it above the site of the ligature occurred by reflux from the vertebral artery through anastomotic vessels around the base of the skull and through the circle of Willis. The cerebral circulation appeared to be maintained by flow through the posterior cerebral artery.

The site of the fistula is in doubt. The possibilities are first, that the original fistula was incompletely tied off, and secondly, that another carotid-jugular communication was overlooked. Leriche (1949) comments on the latter possibility and also points out that the communications between the common carotid artery and jugular vein are usually small, direct and hence give rise to little swelling and pulsation. Another more likely possibility is that a branch of the external carotid artery was damaged at the time of the original injury, the vessel most likely being the superior thyroid artery. In its downward course this vessel could easily be injured together with the common carotid. Most of the other branches of the external carotid artery can be identified on the angiogram and can be excluded. The superior thyroid artery itself has not filled, however. The vertebral artery is unlikely to be affected as at the level of the thrill it appears quite normal in the angiogram and would in any case be lying far back within its bony canal.

As the heart failure has cleared up so well under treatment and the myxœdema has been alleviated it is thought unnecessary at present to close the fistula. This is probably quite small, and may not be the whole cause of the circulatory breakdown.

REFERENCE

LERICHE, R. (1949) Anévrysmes artériels et fistules artério-veineuses. Paris.

**Cruveilhier-Baumgarten Syndrome.**—ELEANOR M. R. TILL, M.B., B.S. (for D. G. FERRIMAN, D.M.).

C. H., male, aged 44.

Admitted to the North Middlesex Hospital on 13.10.53 following hæmatemesis and melæna.

*On admission.*—Hæmoglobin 30%. The spleen was palpable 1–2 fingerbreadths below the costal margin, and the left lobe of the liver was palpable. He was transfused with 5 pints of blood. On re-examination of his abdomen a swelling 1½ in. in diameter was noticed superficial to the xiphisternum

FIG. 1.—Photo to show the venous swelling over the xiphisternum in the patient with Cruveilhier-Baumgarten syndrome.

(*see* Fig. 1): it disappeared on pressure; over it a thrill could be felt and a continuous murmur heard. Between the xiphisternum and the umbilicus were venous varices. The spleen was then 4 finger-breadths below the costal margin. The patient also had acne rosacea, hypotonic muscles and hyper-flexible joints.

*Past history.*—Epileptic fits since he was 14 years. He has never been jaundiced. He does not drink alcohol.

*Investigations.*—Barium swallow showed œsophageal varices. X-ray of chest and skull normal. C.S.F. normal. W.B.C. 3,200. Polymorphs 81%, lymphos. 16%, monos. 2%, eosinos 1%. W.R. negative. Blood group AB, Rh positive. Amino-acid excretion within normal limits (Dr. A. B. Anderson).

Cruveilhier in 1835 and Baumgarten in 1908 described the association of abdominal varices with a patent umbilical vein and congenital hypoplasia of the liver and portal system. Cruveilhier described an abdominal venous murmur. The term Cruveilhier-Baumgarten syndrome has since been applied to the association of portal hypertension, from whatever cause, with an abdominal venous hum and thrill. Visible abdominal varices are commonly but not invariably present (Armstrong *et al.*, 1942).

The mechanism of the hum is not fully understood, but it is probable that a continuous murmur of this nature would be produced by the passage of blood from a high to a low pressure zone as would be found in a free anastomosis between the portal and systemic veins in the anterior abdominal wall in the presence of portal hypertension.

McFadzean and Gray (1953) have described a continuous murmur over the postero-inferior surface of the right lobe of the liver at operation in 5 cases of cirrhosis. In these cases they showed that the murmur was produced as a result of anastomosis between the hepatic arterial and portal venous systems.

The patient stated that the abdominal varices had been present as long as he could remember, and therefore the causes are restricted to those operating congenitally, in infancy or in early childhood. These would include congenital anomalies of the portal veins, bile ducts or the liver itself; syphilis; portal cirrhosis due to infective hepatitis or abnormalities of amino-acid metabolism; and biliary cirrhosis due to congenital obliteration of the bile ducts or obstruction by pigment stones following a rhesus incompatibility state.

POSTSCRIPT (6.3.54)—A lieno-renal anastomosis has since been performed on this patient. Laparotomy revealed cirrhosis of the liver and a patent umbilical vein. Further investigation of this patient is proceeding, and it is hoped to present him at a later meeting of the Society with more detailed information [E. M. R. T.].

## REFERENCES

ARMSTRONG, E. L., ADAMS, W. L., TRAGERMAN, L. J., TOWNSEND, E. W. (1942) *Ann. intern. Med.*, **16**, 113.
MCFADZEAN, A. J. S., and GRAY, J. (1953) *Lancet*, ii, 1128.

[*January* 8, 1954]

**Mitral Stenosis with Multiple Emboli.**—E. S. SNELL, M.R.C.P. (for Professor G. W. PICKERING, F.R.C.P.).

Mr. H. O., aged 38.

*History.*—As a child he had three attacks of rheumatic fever. In 1940 he was rejected for military service because of a cardiac abnormality; occasional dyspnœa on effort at that time. Remained well until 1948 when two attacks of left-sided hemiplegia occurred within three weeks; each was of sudden onset with no disturbance of consciousness. On admission to St. Mary's Hospital, he was found to have a left hemiplegia with auricular fibrillation and signs of mitral stenosis. Radiological examination showed the left auricle to be very large. The hemiparesis improved greatly within three weeks and he was discharged on digitalis.

The first attack of arterial embolism in the legs occurred in 1949 and was followed by further frequent attacks, numbering up to six in one year. Each attack was characterized by a sudden onset of pain, coldness and numbness in the legs with return to normal over the next two weeks. Dyspnœa on effort was present but never very severe. Intermittent claudication in both legs first occurred in 1952. In July 1953 he experienced two attacks of emboli in the legs within twelve days, the second being accompanied by paralysis of the legs and anæsthesia spreading to the waist. Sensation and function recovered in a few days but claudication became severe so that he could walk only a few yards at a time. In addition he noticed impotence for the first time and numbness over the region of the coccyx.

Admitted to St. Mary's Hospital in August 1953. Examination confirmed obstruction of the abdominal aorta; pulsation was palpable at the umbilicus but not distal to this, the buttocks were wasted and the legs were thin, cold and pale. A minimal left hemiparesis was present but no other

neurological abnormalities. There was auricular fibrillation with B.P. 120/70. The signs of mitral valvular disease indicated predominant stenosis; the apical diastolic murmur was loud with an "opening snap" and no systolic murmur. A soft diastolic murmur down the left sternal border was thought to be pulmonary in origin.

*Investigations.*—Radiological examination showed slight systolic pulsation in a left auricle of aneurysmal proportions with enlargement of the right ventricle and to a small extent the left ventricle. ECG confirmed auricular fibrillation and revealed right axis shift. A right carotid angiogram was normal. Exercise tolerance was tested by walking the patient over two steps, each 18 in. high (Hamilton and Wilson, 1952); claudication came on after 7 circuits but dyspnœa was very slight. Reactive hyperæmia of skin (Pickering, 1933) showed on the right side a flush to the malleoli in 40 seconds and to the toes in 50 seconds. On the left side the flush spread to the malleoli in 30 seconds and the toes in 40 seconds (normal time to the toes is 5 to 10 seconds). Aortogram (Fig. 1) by Professor Rob showed a block from below the renal arteries to both common iliacs; the distal vessels were well filled by collaterals. Plethysmography revealed an arterial pressure in the right leg of 55 to 75 mm.Hg. The calf blood flow is illustrated in Fig. 2 and compared with the mean flows obtained from 6 healthy adults. The basal flow was normal but the hyperæmia following a period of five minutes' ischæmia was both reduced and delayed.

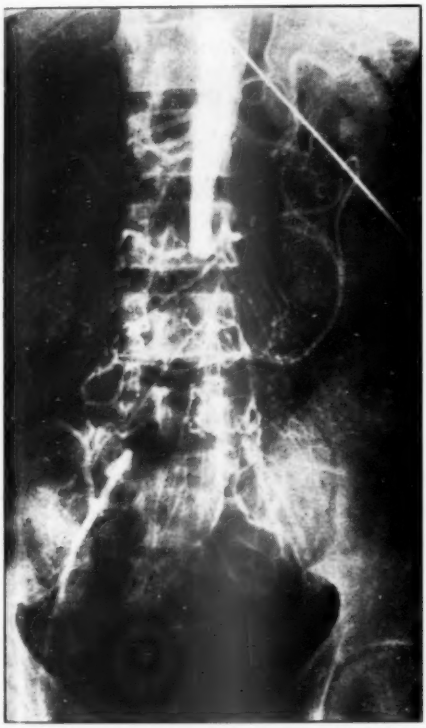


FIG. 1.—Aortogram showing a complete block involving the lower end of the aorta and its bifurcation.

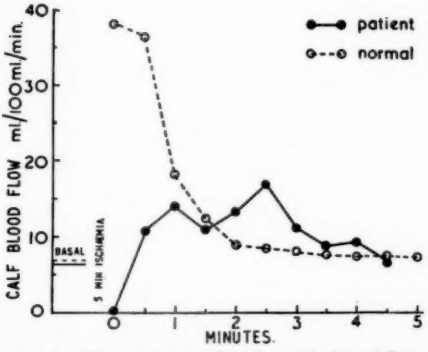



FIG. 2.—The continuous line shows the blood flow through the right calf of the patient before, and immediately after, a period of five minutes circulatory arrest. The interrupted line shows the mean calf blood flow of 6 normal subjects in response to a similar test.

*Discussion.*—Arterial embolus is now generally considered to be an indication for mitral valvotomy. This patient was in peril of involvement of the renal or carotid arteries and it was thought that this consideration took precedence over those features which were unfavourable for operation. Professor C. G. Rob considered that it would be possible to relieve the aortic obstruction by a reconstructive operation. It was decided to perform the heart operation first to diminish the risk of further emboli and improve cardiac function.

*Progress.*—On 14.10.53 Mr. L. Bromley carried out a thoracotomy; pulmonary pressure was moderate and there was no thrill over the left auricle. A finger was inserted into the left auricle, revealing slight regurgitation but no clot. The mitral cusps were not calcified; the orifice was

enlarged by an anterior split from a diameter of about 1 cm. to one of about 2 cm. The auricular appendage was amputated. Recovery was uneventful with no evidence of further emboli. In December 1953 the patient's exercise tolerance was again tested and found to be unchanged, being limited by bilateral claudication. Dyspnœa was even less than previously. If no further emboli occur a reconstructive operation will be performed by Professor C. G. Rob after a prolonged convalescence.

REFERENCES

HAMILTON, M., and WILSON, G. M. (1952) *Quart. J. Med.*, **21**, 169.
PICKERING, G. W. (1933) *Brit. med. J.*, ii, 1106.

**An Unusual Case of Ulcerative Colitis.**—IAN P. TODD, M.D.Toronto F.R.C.S. (for C. NAUNTON MORGAN, M.B., F.R.C.S.).

T. W., aged 45. Occupation: engineering surveyor.

*History.*—1950: Recurrent ulcerative stomatitis.

1952: Vague intermittent low abdominal discomfort.

February 1953: Developed an abscess in the region of the anus, which was treated with penicillin systemically.

March 1953: Onset of diarrhœa, three to four times a day, with blood and slime. Increasing anorexia, malaise and loss of weight.

April 1953: Barium enema suggested sigmoid colitis (Fig. 1). Following the barium enema, the diarrhœa became worse, ten to twelve times a day. A course of succinyl sulphathiazole was given with no effect. Defæcation became painful.

FIG. 1.—Barium enema, April 1953.

*On examination* (27.4.53).—The patient was ill, pale, and had a swinging temperature. The mouth was healthy but the tongue was furred. There was some tenderness in the left abdomen. Rectal examination revealed a deep ulcer just within the anus, but the mucosa of the rectum felt normal.

*Progress* (1.5.53).—Treatment with a low residue, high calorie, high protein diet, with supplementary vitamins, commenced. Penicillin and streptomycin exhibited. There was slight improvement in his condition, and then sudden deterioration with increasing fever and tachycardia, almost continuous diarrhœa and vomiting. The patient became grossly dehydrated. On rectal examination the ulcer had now become a vast fistula and the mucous membrane of the rectum appeared to have been lost. Sigmoidoscopy showed gross purulent ulcerative colitis.

*Operation* (17.5.53).—Ileostomy was performed as a life-saving measure. At operation it was found that the cæcum showed no gross abnormality and the ileum appeared normal on the outside; on opening the ileostomy, however, the ileum was seen to be intensely engorged, œdematous and ulcerated.

*Progress.*—Terramycin was given post-operatively, but the condition did not improve and he developed a purulent bronchitis and ulcerative stomatitis. Swabs from the ileum, mouth and sputum all grew staphylococcus (coagulase positive) which was resistant to all the usual chemotherapeutic agents and antibiotics other than erythromycin.

Erythromycin was given for one week; total dosage 14 grammes. Two days after stopping the erythromycin, the patient complained of pain in the knees and back, suggestive of a toxic arthritis and myalgia.

X-rays showed minimal decalcification of the tibiæ.

The patient's general condition improved only very slowly, though his stomatitis healed, but the pulse-rate remained high and large quantities of purulent material were discharged *per rectum* and through the fistula. Towards the end of June, he complained of increasing low abdominal pain, and his general health deteriorated.

*Operation* (1.7.53).—After pre-operative measures, a subtotal colectomy, bringing out the sigmoid stump on to the abdominal wall, was performed. The whole colon from appendix and cæcum down to the sigmoid showed gross involvement with typical ulcerative colitis (Fig. 2). The small intestine seemed to be completely normal.

FIG. 2.—Segment of colon with mucosal loss, July 1953.

*Progress.*—The patient improved for some time after this operation, but still showed signs of toxæmia and required frequent blood transfusions to combat anæmia.

Nine days after the subtotal colectomy, he developed severe bleeding from the rectal stump, requiring repeated transfusions.

*Operation* (22.7.53).—In view of this, a synchronous combined abdomino-perineal excision of the rectum was carried out. The rectum was found to be surrounded by two huge abscesses.

*Progress.*—Following this operation, the patient developed a severe urinary infection, wound infection and mouth infection, the main organism being once again staphylococcus and also *Bacillus proteus*. The former was sensitive to magnomycin only and the latter was resistant to all antibiotics.

He was given a course of magnomycin with some improvement in his urinary infection, but little effect upon the wounds or stomatitis. His general condition deteriorated in spite of a high protein diet, vitamins and blood transfusions. His weight fell and his wounds continued to break down widely, although they appeared to be clean superficially.

His weight at this time was under 5½ st. (his normal weight was 10½ st.).

24.8.53: Cortisone, 100 mg. a day was started.

This immediately improved his appetite and general sense of well-being and within two weeks he began to gain weight. His face showed the typically fattened appearance due in part to water retention, but his wounds showed evidence of healing. The cortisone was continued for five weeks, at the same dosage, with steady improvement in his general condition.

By October, his temperature had settled, and the wounds were healing rapidly, and at the end of October the cortisone was slowly withdrawn.

3.11.53: He was discharged from hospital with his wounds almost entirely healed, and weighing 8½ stone.

*Comment.*—This case was presented on account of:

(1) The history of preceding ulcerative stomatitis and abdominal pain later associated with ulcers at the anal margin prior to the onset of frank ulcerative colitis. It is suggested that this may fit into one of the triple syndromes such as Behcet's, although no eye signs were present throughout the course of the disease.

(2) The dangers of antibiotic therapy in the treatment of bowel disorders, which, in this case, seems to have caused a resistant staphylococcal septicæmia associated with an enterocolitis.

(3) The use of cortisone. It seems unlikely that this patient would have responded to cortisone therapy in the early stage of the disease. Prolonged toxæmia may lead to depression of adrenal cortical function and in this case the cortisone was given as a form of replacement therapy.

**Mr. David V. Evans:** I can recall a case of ulcerative colitis, which presented with severe and uncontrollable rectal hæmorrhage. This ceased following emergency ileostomy. After total colectomy two years later the patient died from hæmorrhage, which almost certainly was the result of lack of vitamin K.

Regarding the use of cortisone in ulcerative colitis I have been very impressed with the use of ACTH pre-operatively in the seriously ill patient. The number of motions passed each day diminishes and the general condition shows a marked improvement.

**Addison's Disease and Goitre.**—MARGARET E. MORGANS, M.R.C.P.

Mrs. G. J. was first diagnosed as a case of Addison's disease in September 1948, at the age of 40. She gave a three months' history of lassitude, weakness and vomiting.

*Past history.*—Rheumatic fever and pericarditis as a girl. Four pregnancies, all uneventful. She was admitted to the South London Hospital for Women when pigmentation of the skin and mucous membranes and hypotension (B.P. 75/60) were noted on examination.

Investigations revealed serum sodium 287 mg./100 ml., serum potassium 33 mg./100 ml., fasting blood sugar 67 mg./100 ml.; total white cells 6,500/c.mm. (6% eosinophils) and twenty-four-hours' urinary output of 17-ketosteroids 5·9 mg. X-ray of chest was normal, X-ray of adrenal area revealed no calcification and the urine contained no tubercle bacilli. From September 1948 to November 1953 she was treated with DOCA implants. In November 1953 treatment with desoxycorticosterone trimethyl acetate (Percorten-M) was started. At this time it was noticed that the thyroid was considerably enlarged. It was smooth and firm and moved poorly on swallowing. X-ray of the neck confirmed that it was partly intrathoracic, the trachea being pushed forwards, but not significantly deviated or narrowed. The patient was clinically euthyroid. The case notes contain no reference to thyroid swelling prior to October 1952, when the gland was described as "diffuse, soft, moving easily on swallowing". The patient insists that she first became aware of any thyroid swelling only after the onset of treatment for her Addison's disease.

The interest of the case lies in the ætiology of the thyroid swelling, which is of such recent and comparatively rapid onset.

The goitre may be causally related to the Addison's disease or it may be coincidental.

The swelling has only arisen since the onset of the Addison's disease. However, there appear to be no cases of Addison's disease with non-toxic goitre recorded in the literature although occasional cases of thyrotoxicosis are described and pathologically there is said to be lymphocytic infiltration of the thyroid.

Considering the possibility that the goitre is coincidental—it is unusual because of its late age of onset, its clinical characteristics, its fairly rapid increase in size and its behaviour when investigated with radio-active iodine. After a tracer dose of radio-iodine the gland shows a high uptake at one hour and a large part of the iodine is dischargeable with $KClO_4$. This suggests hyperplasia with a partial block of the protein binding mechanism for iodine or a thiouracil-like effect. As can be seen from Fig. 1, this is not the way most non-toxic goitres in this country behave.

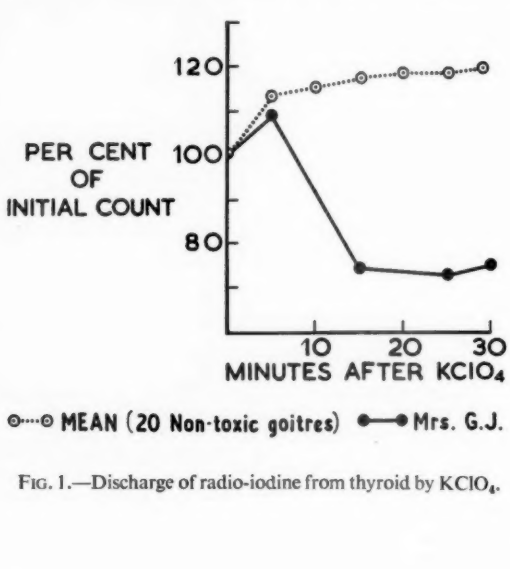



FIG. 1.—Discharge of radio-iodine from thyroid by $KClO_4$.

On questioning, the patient denies taking any drugs at all and the only treatment given for her Addison's disease has been DOCA which is not known to be goitrogenic.

Purely on clinical grounds the gland is compatible with a Hashimoto thyroiditis—it is large, firm and smooth and encircles the trachea. Its behaviour with radio-iodine would also be consistent with this diagnosis—3 cases so investigated with Dr. W. R. Trotter at the Thyroid Clinic at University College Hospital have shown a partial block. This seems to be the most likely diagnosis and it might be tempting to suggest that pathologically the lymphocytic infiltration of a Hashimoto gland could be regarded in this case as an exaggeration of that associated with Addison's disease.

It seems probable that some form of treatment will be necessary to reduce the size of the gland.

It is proposed to administer thyroxine in an attempt to reduce the size of the gland as there is evidence of hyperplasia. Because of the Addison's disease this treatment would have to be started very conservatively.

**Mr. David V. Evans:** The association of changes in the thyroid gland in Addison's disease has been known for many years.

Rossle in 1914 described a case with parenchymatous hyperplasia and Lucksch in 1916 reported a case of lymphoid goitre. Toxic goitre has also been known to occur (Rowntree and Snell, 1931).

Sloper (1953) has described the pathology of the thyroid gland in 21 cases of Addison's disease. 9 of these showed well-marked involutional changes characterized by a varying degree of lymphoid infiltration and fibrosis.

In the case under discussion I would suggest having a biopsy performed.

REFERENCES

LUCKSCH, F. (1916) *Beitr. Path. Anat.*, **62**, 204.
ROSSLE, R. (1914) *Verh. dtsch. path. Ges.*, **17**, 220.
ROWNTREE, L. G., and SNELL, A. M. (1931) A Clinical Study of Addison's Disease. Philadelphia, pp. 72 and 94.
SLOPER, J. C. (1953) *J. Path. Bact.*, **66**, 53.

**Dr. Richard Terry:** If it is decided to treat this goitre by non-surgical means, I should like to suggest that a Vim-Silverman needle biopsy is taken from the thyroid before treatment is commenced.

**Mr. Rex Lawrie** considered it imperative to perform a biopsy of the thyroid in a case of such interest, before commencing any form of treatment.

If the histology resembled lymphadenoid goitre, radiotherapy might be expected to cure it.

**Carcinoma of Cardiac End of Stomach. Abdominal Total Gastrectomy, Splenectomy, Left Adrenalectomy and Partial Pancreatectomy.**—DAVID V. EVANS, M.B., B.S., F.R.C.S.

C. C., male, now aged 52.

*History.*—Admitted to London Hospital, under the care of Mr. Hermon Taylor on 20.5.50. Well until 1947 when onset of dull aching epigastric pain unrelated to meals. Weight: Lost 6 lb. in three years. Now 8 st. 8 lb.

*On examination.*—Anxious man. Tender in epigastrium to left of mid-line. No mass palpable. No ascites. P.R.: n.a.d. No cervical glands.

*Investigations.*—Hb 105%. Barium meal: Moderate-sized projection high up on lesser curve just below cardia. 23.5.50: Gastroscopy: Fleshy red lumpy irregular swelling upper part posterior wall of stomach in centre of which a cavity was indistinctly seen. Appearances were those of carcinoma of the cardia.

*Operation.*—8.6.50: Upper mid-line incision sutured with steel wire. Hard indurated mass about 2½ in. diameter situated just below cardia on posterior wall of stomach involving the hilum of spleen, tail of pancreas and upper part of left suprarenal gland. Radical total gastrectomy performed removing left suprarenal gland, body and tail of pancreas, spleen and omentum. Continuity was re-established by direct end-to-end œsophago-duodenal anastomosis after mobilization of the duodenum and head of pancreas. Pathological report: Solid trabecular polygonal-celled carcinoma of stomach. Secondary carcinoma of two lesser curve glands but no secondaries in remaining glands.

10.6.50: Abdomen reopened for severe central abdominal pain forty-eight hours after operation. Complete volvulus of whole of small intestine. Volvulus untwisted.

21.7.50: Readmitted complaining of dysphagia and retrosternal burning pain. Barium meal: Dilatation of upper loops of jejunum but no narrowing of anastomosis.

October 1950: Readmitted on account of recurrence of symptoms.

5.10.50: Œsophagoscopy: Multiple areas of congestion seen in lower half of œsophagus with small punctate ulcers due to reflux œsophagitis. Œsophago-duodenal junction at 40 cm. was elastic and could be dilated easily with size 21 bougie. Biopsy showed normal mucosa. Continued to vomit. 12.10.50: Laparotomy: Numerous adhesions to parietal peritoneum. Partial duodenal obstruction due to a kink found at point where duodenum passed behind mesocolon. Duodenum proximal to this dilated. No evidence of recurrence. Biopsy of gland in base of mesentery showed chronic inflammatory changes only.

Following this he continued having symptoms of reflux œsophagitis which were controlled with a citric acid/sodium citrate buffer mixture.

27.8.52: Œsophagoscopy: Mild degree of œsophagitis. Solitary pin-head ulcer at 36 cm. No stenosis at anastomosis.

He has continued clerical work and apart from morning retching he has been symptom-free with no evidence of recurrence.

December 1953: Hb 83%. Plasma proteins 6·9 grammes/100 c.c., albumin 4·5, globulin 2·4.

*Comment.*—The fact that this patient has survived over three and a half years following operation in spite of secondary deposits in the regional lymph glands illustrates the important point made by several authors including Swynnerton and Truelove (1952) that the prognosis following resection of carcinoma of the stomach improves with the increasing length of history.

Destruction of the œsophago-gastric valve mechanism following total gastrectomy allows alkaline intestinal juices to regurgitate into the œsophagus. This results in hæmorrhages, erosions, ulceration and later stricture formation of the œsophagus, and gives rise to symptoms such as retrosternal burning pain. It is distressing to the patient and is an important cause of disability following total gastrectomy. The usual remedies such as sleeping in the sitting position were tried without effect. The following citric acid/sodium citrate mixture prescribed by Mr. Sykes, Pharmacist to the London Hospital, resulted in complete relief:

*Dosage:* 2 tablespoons sipped slowly 2 to 5 times daily.

℞

| | |
|---|---|
| Light kaolin | 20 grammes |
| Gelatin | 2 grammes |
| Sodium citrate | 1 gramme |
| Citric acid | 1 gramme |
| Methyl para-hydroxy-benzoate | 0·1 gramme |
| Soluble saccharin | 0·05 gramme |
| Distilled water to 100 millilitres | |

The methyl para-hydroxy-benzoate is a harmless preservative to stop mould which would otherwise grow in the mixture, and the gelatin increases the viscosity slightly and forms a substrate for the intestinal juices to attack in preference to the œsophagus, should the buffering be inadequate.

I am indebted to Mr. Hermon Taylor for permission to report this case.

## REFERENCE

SWYNNERTON, B. F., and TRUELOVE, S. C. (1952) *Brit. med. J.*, i, 287.

**Mr. A. M. Desmond:** It would seem that there is a type of gastric carcinoma which is locally malignant and invades neighbouring structures such as the liver and pancreas, but does not spread early to unresectable lymphatic glands. Wide resection of the stomach and involved organs is sometimes rewarded by long survivals and at St. James', Balham, we have such cases who have survived up to ten years and still remain well.

I have performed the operation of abdominal total gastrectomy with œsophago-duodenal anastomosis eight times with one death. The first case was a woman operated on for hæmatemesis who had an ulcerating leiomyosarcoma of the fundus. She has survived so far two years. Two other cases of small gastric carcinomata requiring urgent surgery for hæmatemesis have been similarly treated with satisfactory results. I have not encountered a case of œsophagitis so far in my series. The indications for the operation I would consider to be:

(1) In the patient of advanced years with a growth not involving the œsophagus nor within 1 in. of it. One case over 80 has now survived for one year.

(2) Any patient with a small growth of the media. I find it difficult to resect a sufficient length of the œsophagus by this route when the cardia is involved and prefer the abdominothoracic approach in such cases.

It is current opinion in this country that peptic ulceration (or œsophagitis) is due to the acid content of gastric juice; but œsophagitis does occur in the presence of hypochlorhydria and even possibly in achlorhydria. In this respect, Winkelmann of Gelsenkirchen, who was assistant to the Surgical Professor at Hamburg, in a personal communication informed me that they believe that stomal ulceration after gastro-jejunal anastomosis is due to the effects of bile and pancreatic juice on the stoma and that they therefore always combine gastrectomy with an entero-anastomosis. He further stated that the incidence of stomal ulceration in 1,500 such operations was 21, i.e. 1·4%. This is very similar to our figures at St. James' where we avoid entero-anastomosis if possible.

One conclusion from this could be that it is the effect of the proteolytic enzymes on a mucosa unaccustomed to them which is the cause. Alternatively the effect of a fluid of high or low pH on such an unaccustomed mucosa may be responsible. This is something which as far as I know has yet to be proved.

# Section of Physical Medicine

President—Doris Baker, M.D., F.R.C.P.

[*December* 9, 1953]

## DISCUSSION: ANTERIOR POLIOMYELITIS

**Mr. Donal M. Brooks** (Royal National Orthopædic Hospital): Poliomyelitis remains one of those diseases for which there is no cure but many different treatments. It is probable that most methods of treatment that are not actually harmful have a measure of success because in the early stages recovery is, to a great extent, spontaneous.

The paralysis which typifies the disease appears either with or soon after a febrile illness. Once the temperature has settled, paralysis ceases to spread unless a further rise in temperature occurs. The subsequent pattern of recovery is well known. Muscles that are initially completely paralysed may or may not recover within a matter of weeks; others that are partially paralysed become progressively stronger until a more or less static phase of muscular recovery is reached. Afterwards, in the absence of any further muscular recovery, there may be a marked improvement in function. There are three broad recovery phases. During the first phase, which extends from the onset to the sixth month, recovery takes place rapidly, reaching its peak at about the third month: this might be described as the phase of neurogenic recovery. In the second phase from the sixth to the ninth month, further improvement in muscles that are already working takes place. Strong muscles improve, weak muscles get stronger, but muscles that have been paralysed at the beginning of this phase remain paralysed—this might be described as the phase of muscle hypertrophy. The third phase of recovery begins about the ninth month and continues indefinitely but most noticeably during the next two years. This latter period is characterized by improvement in general function. Calipers which earlier have proved necessary may be discarded and so on. The characteristic feature of this phase is that, despite careful muscle charting, little significant improvement in individual muscle power can be demonstrated. The improvement in function, therefore, must be due to an improvement in muscle co-ordination and balance.

### Treatment in the Three Phases

Treatment in these three stages differs considerably:

*Phase* 1.—Soon after the onset of paralysis histological evidence suggests that anterior horn cells are either completely destroyed by the action of the virus or may, as Bodian (1947) has claimed, undergo reversible changes which lead, for a time, to a suppression of function. At this stage, the degree of paralysis may be far in excess of that which can be accounted for by obvious cell damage in the cord; on the other hand after six months the degree of paralysis may be closely correlated with the extent of cell destruction in the cord. Œdema of the cord which gradually subsided used to be offered as an explanation for the rapid recovery which occurs during this phase, but this is not borne out by histological work. There are two further possibilities: Firstly that transient reversible changes in the anterior horn cells as suggested by Bodian result in a temporary loss of function, in the absence of any axonal degeneration, so that, when cell stability is regained, normal function is restored. Secondly that severe but reversible changes in the anterior horn cells occur which lead to a limited peripheral degeneration of the axons with subsequent regeneration over a very short distance following recovery of the parent cells (Seddon, 1949).

In an attempt to gain further information about the state of the lower motor-neuron during this phase, we carried out some electrical investigations (Brooks, 1953). Previous work and experience ruled out the possibility of axonal regeneration occurring in the same way as it does after peripheral nerve injuries. It was felt, therefore, that a prognosis for completely paralysed muscles might be confidently expressed if it could be established whether or not the paralysis was due to a degenerative lesion of the lower motor-neuron.

Three methods of investigation suggested themselves:

(1) Strength or intensity duration curves.

(2) Electromyography.

(3) Nerve conduction.

While all these methods provide a means of establishing the integrity or otherwise of the lower motor-neuron, in clinical practice there are certain disadvantages peculiar to each.

(1) *Strength duration curves.*—The curves so obtained provide information concerning the degree of innervation of a particular muscle. In a muscle that is partially denervated, a compound curve consisting of a combination of the reaction of normal and denervated fibres is found. McKenzie (1949), in his paper on "The value of strength duration curves in prognosis in poliomyelitis" concluded that the partially denervated muscle had a better prognosis—which agrees with clinical experience. The method is time-consuming in patients with extensive paralysis; moreover, it is not completely reliable unless the muscle bulk is small, as in the intrinsic muscles of the hand. When the muscles of the thigh and buttock are investigated in this manner, only those fibres subjacent to the electrode can be examined with certainty.

(2) *Electromyography.*—For satisfactory recording intramuscular needle electrodes must be used. For certain investigations, surface electrodes are adequate but will not pick up fibrillation action potentials. As a routine clinical procedure, needling is not practicable for children and is exceedingly unpleasant for adults. Furthermore, when using needle electrodes only a small area of muscle can be examined at any given time unless multiple needling or extensive probing is resorted to. Muscles in poliomyelitis are rarely completely denervated, in striking contrast to those paralysed following nerve section. Erroneous information can be gained, therefore, unless the examination is thorough. Moreover, the interpretation of recordings obtained by this method can be confusing. For example, complex polyphasic action potentials that herald the re-innervation of muscles following nerve suture have been shown by Bauwens and others to have no such significance in poliomyelitis. For the time being we feel that the prognostic value of electromyography is uncertain.

(3) *Nerve conduction.*—By nerve conduction is meant the percutaneous stimulation of the main nerve to a muscle or group of muscles with an electrical stimulus of a relatively short duration—1 to 10 milliseconds. The presence of a significant number of intact motor-units is demonstrated by a visible strong or weak contraction or, where all have perished, no contraction at all. This method has the advantage of being relatively painless by reason of the character of the stimulus, moreover, it is quickly and easily performed. It seemed, therefore, to be the method of choice. Its sole disadvantage lies in the fact that the nerve must be superficially placed.

This method was used in over a hundred cases. It is important to emphasize that only those muscles that were clinically *completely* paralysed were examined. Quite a number of the electrical investigations were carried out within the first three weeks of paralysis and the vast majority within six months. Two groups of results were obtained.

In most instances, as might be expected, clinical paralysis was associated with a lack of response to nerve stimulation, but in almost a quarter of the cases a significant response was obtained within the normal threshold stimulus. By a significant response, we mean a muscular contraction sufficiently powerful to cause a movement of the relevant joint against gravity. Now, in those cases in which there was a loss of nerve conduction, it seemed reasonable to suppose that axonal degeneration, secondary to cell destruction, had occurred and that no recovery might be expected. However, recovery in some of these muscles did occur within the first six months of the disease. The time at which recovery occurred, however, bore no relation to the distance of the muscles from the cord, thus proximal muscles did not recover before those situated more distally. In other words, there was no evidence that complete axonal regeneration from the anterior horn cells could have taken place. Our knowledge of the way in which axonal degeneration following nerve section takes place is fairly complete. It has been shown, on many occasions, that degeneration occurs simultaneously at all points along the nerve distal to the site of damage. It is possible that this classical mode of degeneration may not take place in a nerve fibre which is in anatomical continuity with its cell and in which the cell has sustained sublethal damage—such as occurs in poliomyelitis. If it were reasonable to suppose that the axons of those cells which are partially injured undergo a limited centripetal degeneration, as has been suggested by Carey (1943), then in the event of cell recovery,

the short distance necessary for axonal regeneration would lead to an early restoration of function. It may be, however, that transient changes in the cell can result in a disturbance of transmission at the myoneural junction in the absence of any axonal degeneration. This also would account for recovery of voluntary power where nerve conduction had, at one time, been absent.

In the second group, those cases in which nerve stimulation evoked a significant response, it was argued that as a considerable number of axons were intact and presumably anterior horn cells, some recovery might be expected; in most instances, this proved to be correct. The site of "block" in these instances might be located in the cell itself; the findings of O'Leary *et al.* (1932) lend support to this notion. Alternatively, the block might occur proximal to the anterior horn cell, somewhere between it and the termination of the upper motor-neuron, in perhaps an internuncial neuron, or possibly higher still in the facilitatory centre in the brain-stem. Lastly, there was a small number of cases who failed to recover despite a favourable nerve conduction result, and in which on repeating nerve conduction at a later date, no response was elicited.

## Conclusions

(1) There is often a true functional (non-degenerative) paralysis in the early stages of an attack of anterior poliomyelitis which may persist for as long as four months.

(2) Such a functional paralysis does not always carry with it a good prognosis and may become a degenerative paralysis.

(3) Evidence of a degenerative paralysis within the first six weeks does not always mean a bad prognosis.

(4) The results of nerve conduction examination after the sixth week, in most instances, provide a sound basis for a prognosis.

### *Treatment in Phase* 1

The aims of treatment in poliomyelitis are: To save life; prevent deformity; restore function; and to rehabilitate.

The first two are important in phase 1. Life-saving measures are related to treatment of paralysis of the respiratory and swallowing muscles. Few artificial respirators provide adequate ventilation and, at the same time, enable physiotherapy to be carried out. Tracheotomy offers one solution, but it is a desperate measure that should only be resorted to in desperate circumstances.

*Deformities.*—The two most important causes of deformity are: (*a*) Faulty posture. (*b*) Muscle imbalance.

Postural deformities should never be allowed to develop but the common deformities of drop foot and back knee are still seen far too frequently. They can be prevented by early passive movements and by using simple supports between treatments which maintain the knee in slight flexion and the foot at a right angle. Postural deformity, of course, may be secondary to pain, with the result that the limb is placed in the position that is the most comfortable but which may predispose to contracture. There are three distinct types of pain: spontaneous, that induced by stretching muscle, and lastly muscle tenderness. Spontaneous pain is rarely a serious complication and does not last for long. Similarly muscle tenderness, although not infrequent, does not interfere with treatment. Pain on muscle stretching can be a great problem. It is this feature which has given rise to so much discussion of "muscle spasm". It can only affect those muscles that are not completely paralysed and where adequate passive movements have been given from the onset it is not often seen. It is a phenomenon that varies with different epidemics and usually regresses with physiotherapy. Where it is persistent it may be relieved by hot packs and sometimes sympathetic paralysants.

Whereas in adults postural deformity can be prevented by adequate passive movements and simple measures, in children a more rigid type of splintage is often advisable. A most insidious deformity is caused by shortening of the tensor fascia lata from continued adoption of the frog position which is common in infants. In these instances Seddon's "Mauritius" splints are very useful (Fig. 1), particularly if the child is made to lie prone for part of the day with the splints in position (Fig. 2).

*Splintage.*—Our use of splintage in paralytic disorders is quite inconsistent. For example, in injuries of the radial nerve it is common to supply some form of cock-up splint which may or may not incorporate an extensor apparatus for the fingers. Yet in a median nerve palsy no such splintage of the wrist or of the fingers in flexion is resorted to. Again, in a complete sciatic nerve lesion, a toe-raising apparatus is supplied to enable the patient to walk. This must obviously favour the dorsiflexors of the foot and put the calf muscle under tension. Curiously enough, recovery in the calf muscle is consistently better than in the dorsiflexors after sciatic nerve suture. The conclusion that must be reached is surely that recovery of voluntary power occurs provided the nerve suture has been successful and not because the muscles have been maintained in a relaxed position. Now, if we apply this reasoning to poliomyelitis, is there any good reason for supplying an abduction frame in cases in which there is a paralysis of the deltoid? Can continued relaxation of the deltoid affect its recovery in any way, *provided* that adequate physiotherapy is being carried out? My impression

is that in some instances it may even do harm, because if the arm is kept elevated on an abduction frame the use of the limb is seriously curtailed. Moreover, any encouragement for the deltoid to work is automatically removed. A recent review by my colleague Sharrard (1954), of cases of deltoid paralysis treated with and without abduction frames confirms these impressions. It is still a familiar sight to see an unfortunate sufferer from poliomyelitis wandering about with his arm in an abduction frame more than a year after the onset of paralysis in the forlorn hope that this treatment will in some mysterious way cause the muscle to recover. I feel sure there are only two indications for using splints in poliomyelitis: to prevent deformity, and to improve function.

FIG. 1.—Child in "Mauritius" splints which control the tendency for it to assume the natural "frog" position.

FIG. 2.—Child lying prone in "Mauritius" splints.

*Phase* 2.—By the end of four months the pattern of residual paralysis is established. It is at this stage, therefore, that physiotherapy should concentrate on individual training of those muscles that have been spared, by means of graduated exercises incorporating progressive resistance.

Regular muscle charting is an essential guide to progress, and is particularly valuable in this second phase of the disease. The most useful system of grading and recording muscle power is that adopted by the Medical Research Council in 1943 (Table I), based on the method advocated by Lovatt in

TABLE I.—MEDICAL RESEARCH COUNCIL SYSTEM OF MUSCLE GRADING (1943)

0. No contraction.
1. Flicker or trace of contraction.
2. Active movement with gravity eliminated.
3. Active movement against gravity.
4. Active movement against gravity and resistance.
5. Normal power.

1912. It is sometimes suggested that greater accuracy in measuring and recording muscle power could be achieved by the use of spring balances and other similar devices. But as in manual methods of muscle testing, in attempts to achieve greater precision, practicability often yields to complexity.

Mechanical means of measuring and recording muscle power should be reserved for research purposes rather than for routine work. Muscle charts in general are either too detailed or not detailed enough. Recently we have tried to combine a chart which gives details of individual muscles and yet provides some indication of the function of the limb as a whole. In it muscles are grouped together in regard to the movement they produce and not to their innervation (Table II). While it

TABLE II.—SPECIMEN OF MUSCLE CHART DESIGNED TO EXPRESS FUNCTION AS WELL AS INDIVIDUAL MUSCLE POWER

Forearm and Hand

| | Right | Left |
|---|---|---|
| Extension of forearm | | |
| Triceps | | |
| Flexion of forearm | | |
| Brachialis<br>Brachioradialis<br>Biceps | | |
| Supination of forearm | | |
| Supinator | | |
| Pronation of forearm | | |
| Pronator teres<br>Pronator quadratus | | |
| Extension of wrist | | |
| E.C.R.L.<br>E.C.R.B.<br>E.C.U. | | |
| Extension of digits | | |
| E.C.D.<br>E.P.L.<br>E.P.B.<br>E.I. | | |
| Flexion of wrist | | |
| F.C.R.<br>P.L.<br>F.C.U. | | |
| Flexion of digits | | |
| F.D.P.<br>F.D.S.<br>F.P.L. | | |
| Opposition of thumb | | |
| A.P.L.<br>A.P.B.<br>F.P.B.<br>O.P.B. | | |
| Mass intrinsic action | | |
| D.I. 1, 2, 3 and 4<br>P.I. 1, 2, 3 and 4<br>Hypothenar muscles<br>Adductor pollicis | | |

may often be possible to order permanent supportive apparatus from the muscle chart, on occasions this can be dangerous; the muscle chart may either over- or under-estimate the patient's capabilities and instruments may be ordered which subsequently prove unnecessary. To avoid such waste of time and money it is wise to give all doubtful cases a trial of walking, in which the lower limbs are braced by removable back-slabs and a simple toe-raising apparatus is fitted (Fig. 3). If walking in

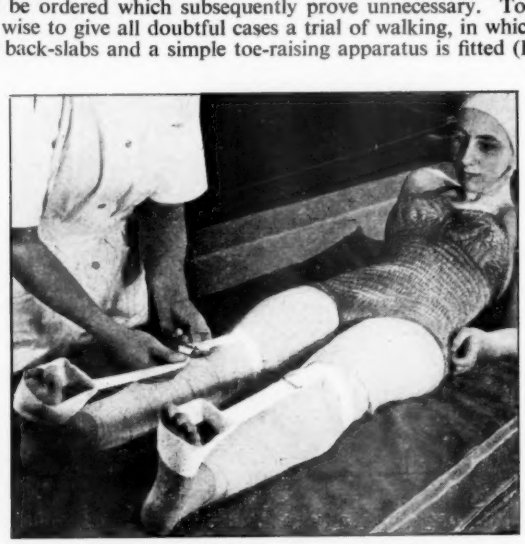


FIG. 3.—Showing plastic back splints and simple toe-raising apparatus being adjusted before patient starts a "trial of walking" in the swimming pool.

the pool is successful they then progress to walking between bars in the gym. If the trial proves successful, then, and only then, is definitive apparatus ordered. If unsuccessful, it is the kindest and most reasonable way to impress on patients that they are unable to walk on account of the severity of their paralysis rather than to tell them outright that they will never walk again. Besides, we do not always know.

About this time the second type of deformity, that due to muscle imbalance, becomes apparent. When muscle imbalance is marked, external supportive apparatus can do little to prevent a deformity from developing. Those who have watched the development of a paralytic scoliosis know well how ineffective jackets can be—similarly how difficult it is to maintain a foot with an isolated paralysis of the peronei in the plantigrade position no matter how elaborate the instrumentation may be. It is in some of these instances that balancing operations incorporating tendon transplantation can do much to help. It should be stressed that the development of structural deformity from muscle imbalance is essentially a phenomenon of childhood and not one that is seen after bone growth has ceased.

*Phase* 3.—At a certain stage muscle charting shows that improvement in muscle power has come to a standstill. At this stage, physiotherapy should be concentrated towards improving the functional capacity of the patient. For example, they should be taught to go up and down stairs, get in and out of a wheelchair, bath, &c. Individual muscle training should play no part in this part of the programme of treatment. As soon as it is possible treatment as an in-patient should cease, and under ideal conditions, the adult should be transferred to a Rehabilitation Centre. If this cannot be arranged then he will have to be discharged home and continue treatment as an out-patient. In either case, there must be the stimulus to compete with everyday life away from a hospital atmosphere. At Stanmore we are particularly fortunate in having Garston Manor so near. Here Group Captain C. J. S. O'Malley and his team produce the most dramatic improvement in function within a relatively short time. The right family environment can also help to complete this final phase of recovery. An unnecessarily prolonged stay in hospital or a return to an over-sympathetic household may prejudice the final degree of recovery reached.

In children out-patient treatment should be combined, where possible, with schooling, and in this connexion segregation in P.H. schools should be avoided. Sooner or later these children will have to mix freely with their fellow creatures and a sheltered existence in childhood must make this more difficult later on. Regular follow-up must be continued indefinitely. The patient with poliomyelitis should never be finally discharged.

In adults rehabilitation cannot be considered complete until the patient is established in remunerative employment. Nowadays industry is much more tolerant towards the physically handicapped, and in our experience is very willing to co-operate with resettlement problems. We are fortunate in having the services of a Hospital Resettlement Officer who acts as a liaison officer between the hospital, industry and the D.R.O. Personal contact with employers is vital. No amount of writing can be a substitute for a visit.

Lastly, there is the problem of the severely paralysed young adult who cannot return home and will not be accepted by a Rehabilitation Centre. The facilities for caring for such patients are totally inadequate. Banishment to a hospital for young chronic sick is, at present, the only available solution for these people. Much money has been and is being spent on developing Rehabilitation Centres. It is high time that this small, but none the less important group of patients should have the comfort and care which they deserve.

## REFERENCES


BODIAN, D. (1947) *J. Amer. med. Ass.*, **134**, 1148.

BROOKS, D. M. (1953) The Spinal Cord (Ciba Foundation Symposium). London.

CAREY, E. J. (1943) *Proc. Soc. exper. Biol., N.Y.*, **53**, 3.

MCKENZIE, I. G. (1949) *Proc. R. Soc. Med.*, **42**, 488.

Medical Research Council (1943) M.R.C. War Memorandum No. 7. H.M. Stationery Office.

O'LEARY, J. L., HEINBECKER, P., and BISHOP G. H. (1932) *Arch. Neurol. Psychiat., Chicago*, **28**, 272.

SEDDON, H. J. (1946) *Lancet*, ii, 707.

—— (1949) Poliomyelitis: Papers and Discussions presented at the first International Poliomyelitis Conference. Philadelphia; p. 34.

SHARRARD, W. J. S. (1954) Unpublished work.


**Dr. W. Ritchie Russell** (Department of Neurology, Radcliffe Infirmary, Oxford): All methods of treatment in modern medicine should be submitted to properly controlled trial, and the main theme of my few remarks is that this vital principle has not yet been sufficiently applied to the treatment of poliomyelitis. The result is that the value of almost every suggested method is disputed by someone, not because he has tried it but because he has always done something different.

To a research worker this is an unacceptable state of affairs and it is obviously now necessary to collect accurate information as to the pattern of recovery with the various methods of treatment in common use.

The first consideration must be to save life, and there are two things to watch for specially: (1) paralysis of swallowing; (2) weakness of respiration, speaking or coughing. It is obvious that everything must be subordinated at first to the task of keeping the airways clear.

In bulbar paralysis where there is paralysis of swallowing, proper posturing is the key to success. A firm flat mattress without pillows is the first requirement. Lying on the back (supine) is always dangerous in these cases, and the best positions are the right and left semi-prone and right and left lateral with the foot of the bed raised for extra drainage as required. An inverted "V" bed is specially useful for the full prone posture. Every breath should be listened to by a nurse trained to recognize when secretions are accumulating and to deal with them by suction and posturing. A throat microphone connected to a loud speaker is useful for this (Stott, 1953).

The posture must be changed through a wide angle every two hours, and at this time a period of assisted expiration by pressure-vibration on the chest is most valuable in keeping the lungs free of obstructing secretions. Where physiotherapists are not sufficiently available throughout the twenty-four hours then doctors and nurses should do what they can every time the posture is changed. A doctor must in any case be on immediate call to assist with respiratory difficulties and to do a tracheotomy should this become necessary. Splinting of any kind gets in the way and should not be used in bulbar cases.

### RESPIRATORY PARALYSIS

Failing respiration is recognized easily by those familiar with the disease. It is best to start respirator practice before the patient is seriously embarrassed, and an expert team can put a patient in a modern respirator without either physical or psychological trauma. Physiotherapists are a valuable addition to any such team. The idea (not entirely extinct) that in trunk paralysis the patient should be supported in some form of rigid bed or frame is dangerous, for the most important part of treatment in the early days of respiratory weakness is again to posture the patient to keep the lungs healthy. As a bare minimum the patient's posture should be changed every two hours with full use of the lateral and semi-prone postures. Each time the posture is changed the uppermost part of the chest in the new posture may with advantage be treated by the physiotherapist and firmly compressed (to toleration) during expiration to reduce the risk of atelectasis. There is a persistent tendency to leave these patients lying on their backs in the acute stage of the disease, but this is dangerous and leads to many fatal lung complications.

While the patient's survival is in doubt all efforts must be directed towards keeping the air passages clear, and the lungs healthy. At this stage splints and hot packs are likely either to get in the way or divert attention from vital measures required to save life.

The best way to check on the state of respiratory paralysis is to measure the vital capacity with a spirometer. I have been told on several occasions by physiotherapists that hot packs to the chest improve respiratory excursions of the chest in the acute stage of the disease and may avoid the need for iron lung treatment. If this is really so, then it should be easy to demonstrate by measurement with a spirometer: my experience of these cases hardly suggests that hot packs provide a serious contribution to the critical problems which develop so quickly. In any case the skilful use of a respirator will give the muscles of respiration the best possible rest, and will counteract any tendency to lung collapse better than anything else.

In the modern respirator with a split front (Russell, 1952) the patient can be nursed in the semi-prone posture, and his position can be changed every few hours: this frequent change of posture seems to be a most important part of the effort to keep the lungs healthy.

In some cases with combined paralysis of respiration and swallowing the Copenhagen method (Lassen, 1953) of positive pressure breathing seems the method of choice. These cases are specially liable to lung collapse: here chest physiotherapy is essential, and may be applied day and night at the vital two-hourly changes of posture. An easily tilted bed is specially useful for this type of case (Fig. 1).

FIG. 1.—Physiotherapy applied to the chest of a patient recovering from respiratory paralysis which had been treated by positive pressure breathing through a cuffed tracheotomy tube (Russell and Schuster, 1953).

While these struggles go on to keep the patient alive the only treatment that can be given to muscles of the limbs is posturing with pillows and passive movements, and these are good reasons for advising absolute physical rest and heavy sedation during the acute stage of the disease. Here we at once meet with differences in practice, for some advise the avoidance of passive movements in the early days of the disease, others push them vigorously from the first day of the disease, and others again apply them once or twice daily after applying hot packs. Our practice is to give gentle passive movements every four hours day and night from the first day of the disease, and the nurses are trained to do

these during any of the four-hour periods at which a physiotherapist is not available. We generally have little time to use hot packs, and have had little serious trouble with muscle tightness—any we have had was due to our own failure to notice that some muscles were being overlooked.

It is perhaps obvious that muscle tightness after the paralysis has fully developed is an entirely favourable sign as regards the affected muscle, as tight muscles at this stage make an excellent recovery. A muscle which loses its reaction to nerve stimulation at ten days is never tight at this stage. The brisk electrical responses in the acute stage of muscles which are permanently paralysed indicate how very mistaken was the view advocated by Sister Kenny that the disease affects especially the muscles. It would indeed be wonderful if poliomyelitis were a disease of muscle, as necrotic muscle regenerates very well, while this is impossible for the anterior horn cells.

### Muscle Spasm

"Muscle spasm" is rarely a troublesome feature when passive movements have been used from the onset of the disease, but I don't think that once or twice a day is enough: hence the need for nurses to be trained to move joints day and night. If limbs are left unmoved for a few days, then muscle tightness develops very quickly in muscles which are allowed to lie in a shortened position, as happens when an active muscle is opposed by a much weakened or paralysed group. This is a well-known physiological effect and is by no means peculiar to the paralysis due to poliomyelitis. Exactly the same phenomena may occur in cases of nerve injury where the limbs have been inadequately mobilized, or left in a position which allowed a healthy muscle to shorten. Muscle tightness is evaluated very differently by different people, and there is some uncertainty as to how far the very full range of mobility insisted on by some is necessary. It is often maintained that even slight muscle tightness of one muscle group leads to serious interference with recovery of antagonists. There is no satisfactory evidence on this point but the matter could obviously be assessed accurately by careful measurement of muscle strength.

The worst problems are concerned with cases in which the pattern of the paralysis causes gross imbalance of opposing muscle groups, as the unopposed group inevitably tend to shorten, and it is here that some lively form of splint to counter the strongest group seems to be specially valuable. For example, the use of slings supported by springs is specially valuable in case of deltoid paralysis.

I think that much of the confused thought about polio is caused by the fact that many doctors and physiotherapists specially concerned with rehabilitation treat only the recovering stages of the disease, and I suggest for your consideration that physiotherapists should be seconded voluntarily from large physiotherapy centres to hospitals admitting acute cases. Only by treating all stages of the disease in different ways can one hope, for example, to understand the various factors which determine prognosis, and those which limit the possibilities of treatment.

After three or four weeks, what then? Obviously the rate of rehabilitation should be planned to get the best final result, but how are we to compare the various methods that are used? There is, for example, a widespread belief that rest in bed for several months is beneficial to the proper recovery of the trunk and pelvic girdle muscles, but in fact there is little evidence to support this view. My own impression is that everything possible should be done to encourage movement, and where the upper limbs and shoulder girdles are strong, early exercise in the erect posture is beneficial, as the body weight can be sufficiently supported by the upper limbs. When the upper limbs are also weak, then many difficulties arise, and in order to encourage freedom of movement upright exercises by supporting the body with a harness or under water are helpful. Periods of freedom of action may also be supplied by allowing the children to roll about on several mattresses placed together. However, the long-term care of these cases provides special difficulties. We have treated our cases on the view that unrestricted movements after the first three weeks are safe for most cases under certain conditions. For example, we encourage standing and walking exercises under supervision within five weeks of the acute stage provided that the weight can be properly supported by the arms or other means if the legs and trunk are weak or paralysed.

Here I should like to refer to the remarkable study of individual muscle retraining practised by some very expert and experienced physiotherapists, as seen best perhaps in the elaborate muscle work done in Australian clinics. I always find this detailed knowledge and muscle training most impressive but nevertheless it seems to me probable that much of it is unnecessary. There are only a very few trick movements which are undesirable, for most represent the rational compensation of the spinal cord for what has been lost, and the idea that we know better than the spinal cord how to reorganize its resources seems to me to be extremely improbable. Here again it should be possible to compare different methods in order to adjust the wide variations in practice which are now apparent.

One essential in attempting to assess the merits of various methods of dealing with muscles is to have some system of measurement. The 0–5 method may suffice for the almost completely paralysed, but it is not sufficiently accurate for most purposes. Dr. Fischer-Williams and I have found the old method used forty years ago by Lovett and Martin (1916) to be entirely appropriate for this type of study. This consists of a simple sling and spring balance, but for some observations we have found a recording dynamometer (Russell, 1952) to be specially useful to make a record of the rate of fatigue

as well as of maximum strength. Dr. Fischer-Williams and I have measured the strength of certain muscle groups during recovery from poliomyelitis for periods extending to over a year in some cases. (The slides shown by the speaker are reproduced in the *Lancet*, Russell and Fischer-Williams, 1954). Under the conditions observed these slides show that improvement in voluntary muscle power begins within two weeks of the appearance of paralysis and progresses very steadily for about nine months. Thereafter progress becomes very slow or ceases entirely. These slides are from unselected cases, and we have no records of muscle strength being lost from even deliberately induced fatigue.

Early inactivity or splinting will delay the start of this improvement, but whether the ultimate result is better or worse is not known. I believe that curves of this type can be established for all forms of treatment, and I would urge those who treat poliomyelitis to record the progress of certain muscles in this way. By this means all forms of treatment can be compared with each other quite reliably.

It is also necessary to experiment with different methods, (for charts *see* Russell and Fischer-Williams, 1954) we have tried to over-fatigue certain muscle groups in order to observe the much-publicized dangers of fatigue. This experiment involves no risk to the patient under careful supervision, and we have so far failed to reproduce the harmful effects which are alleged to follow fatigue. In a few cases these intensive exercises were followed by an acceleration of recovery, and this perhaps indicated some inadequacy of the rate of the preceding rehabilitation.

These curves of recovery are difficult to explain. Clearly there is no step in the curves which would indicate nerve regeneration, and it is hard to accept the view that muscle and nerve hypertrophy accounts for all recovery that occurs. It seems probable that much of the recovery depends on reorganizing central pathways to allow isolated motor neurones to resume control by voluntary action. The organization of the spinal cord is much more plastic than was considered possible at one time (Eccles, 1952), so that it may be best to consider much of the improvement as merely a return of central control of spinal neurones. For this type of recovery the patient's own determined attempt to move is likely to be the most powerful stimulus available, and indeed there are many examples known to us all of the surprising effects of individual determination in cases of poliomyelitis.

We have been careful not to allow much weight-bearing. Excessively vigorous stretching of muscles which have been allowed to shorten and thus become "tight" may not only weaken them, but may actually precipitate the dangerous calcifying myositis.

It is most important that the best rate of rehabilitation should be established, as this influences profoundly the duration of hospital treatment of certain types of case. In many clinics patients with weakness of the trunk and pelvic girdle muscles remain in hospital for as long as eighteen months or two years. In contrast to this, we have allowed several such patients to go home under out-patient supervision within three or four months of the onset of the disease, and we have as yet no evidence to indicate that this has done harm—indeed the rate of muscle recovery often quickened after going home.

It is difficult to compare the experience of different centres, as many of the best known admit cases which are selected for their severity or difficulty. Further, it is obvious that liberties can be given to intelligent adults which would be dangerous for small children. For statistical purposes, it is better to study all the cases in a single outbreak as we were able to do at Stoke Mandeville in 1952, when both the acute and the rehabilitation stages were treated by the same medical physiotherapy and nursing staff—an arrangement which has so many obvious advantages that I think it should be more widely adopted.

In 1952 we had 50 paralytic cases at Stoke Mandeville Hospital, including 5 bulbar and 1 respirator case. Thirty-four left hospital within 12 weeks, eleven at from 12–28 weeks after the acute illness, leaving only four children requiring a longer period (over 7 months) of hospital treatment. Much of course depends on the home conditions, especially in the case of children, and in at least one case the out-patient supervision proved to be inadequate owing to transport and other difficulties. It is quite clear that some severely disabled children require long years of hospital treatment when home conditions are inadequate for the problems involved, but when home conditions are good the psychological effects of removing young children from home for long periods should be carefully considered in relation to the plan of treatment.

## REFERENCES

ECCLES, J. C. (1952) The Waynflete Lectures. Oxford; Chapter 6.
LASSEN, H. C. A. (1953) *Lancet*, i, 37.
LOVETT, R. W., and MARTIN, E. G. (1916) *J. Amer. med. Ass.*, **66**, 729.
RUSSELL, W. R. (1952) Poliomyelitis. London.
——, and FISCHER-WILLIAMS, M. (1954) *Lancet*, i, 330.
——, and SCHUSTER, E. (1953) *Lancet*, ii, 707.
STOTT, F. D. (1953) *Brit. med. J.*, ii, 1414.

# Section of Endocrinology

President—RAYMOND GREENE, M.A., D.M., M.R.C.P.

[*November* 25, 1953]

**Scleroderma with Symmetrical Periarticular Calcinosis.**—RAYMOND GREENE, D.M.

This case is to be published in full elsewhere.

**Bilateral Adrenocortical Hyperplasia with Cortical Adenoma.**—D. FERRIMAN, D.M., M.R.C.P.

E. M., female. Seen in Outpatients July 1950, aged 49.

*Complaint* was of obesity. Obesity and œdema of legs ten years. Change in facial appearance and pains in chest and groins seven to eight years. Amenorrhœa four years. Hirsuties and easy bruising two years.

*Examination* revealed an obese, plethoric moon-faced woman. Facial hirsuties. B.P. 230/120. Glycosuria. Few pale pink abdominal striæ distensæ. Pitting œdema of legs and feet.

Glucose tolerance test: Fasting, 89 mg./100 ml., 0 hours; 240 mg., ½ hour; 240 mg., 1 hour; 214 mg., 1½ hours; 177 mg., 2 hours.

FIG. 1.—E.M., 28.11.50.

FIG. 2.—E.M., 23.11.53.

X-rays thoracic cage, lumbar spine, pelvis: Some osteoporosis. Fractures of ribs and pelvic bones. Calcification in capsule of pelvic tumour.

17-ketosteroid excretion (Dr. A. B. Anderson): 27, 28 and 29 mg./24 hours. Serum calcium, phosphorus, alkaline phosphatase, sodium and potassium and plasma chloride within normal limits.

*Operations* (Mr. K. A. K. Hudson).—10.7.51: Removal of left ovarian fibroma and right ovary. No improvement. 17-ketosteroid excretion 23 mg./24 hr. 16.10.51: Removal of 9/10 left suprarenal. Weight 14 grammes. Some temporary improvement. 17-ketosteroid excretion 16.1.52, 9·7 mg./24 hr.; 26.9.52, 14·4 mg./24 hr. 10.3.53. Removal of 7/8 right suprarenal—this consisted almost entirely of an adenoma, weight 9 grammes.

Patient has shown a definite improvement in facial appearance (*see* photographs). Facial hair is

now fair and growth has ceased. She has lost 1½ st. in weight. B.P. 180/90. Trace of œdema still. G.T.T.: Fasting, 115 mg./100 ml.; 188 mg., ¾ hour.; 190 mg., 1½ hours; 177 mg., 2 hours. 17-ketosteroid excretion 7 mg./24 hr.

The interesting feature about this case is the association of a large cortical adenoma with adrenal cortical hyperplasia.

**Cushing's Syndrome.**—R. I. S. BAYLISS, M.D., M.R.C.P., and J. B. HUNTER, M.B.

J. L., aged 23, lorry driver.

Admitted 3.11.53. For six months had noticed increasing fatness of face and trunk, falling scalp hair and mild mental depression. For three weeks before admission he had observed striæ on the thighs and upper arms and a falling off in potency.

On admission he had typical plethoric "moon" facies with truncal obesity and a "buffalo" hump. The skin was dry with mild acne and marked purple striæ on thighs and upper arms. No ecchymoses were seen. The initial blood-pressure was 230/120 but this fell after several days' rest to 160/110. Urine contained neither albumin nor glucose.

*Investigations.*—Hæmatocrit 46·5%. Circulating eosinophils 50 per c.mm. Plasma electrolytes normal. Glucose tolerance test (50 grammes glucose): 72 mg. per 100 ml., 0 hours; 92 mg., ½ hour; 152 mg., 1 hour; 180 mg., 1½ hours; 121 mg., 2 hours.

X-rays of skull, chest, and spine normal.

Air insufflation showed nothing abnormal, adrenals appearing of normal size.

Urinary 17-ketosteroid excretion 35 mg. per 24 hours (mean of seven determinations). Plasma 17-hydroxycorticosteroids 24 µg. per 100 ml. (upper limit of normal 18 µg. per 100 ml.). An eight-hour intravenous infusion of 20 units ACTH raised the urinary 17-ketosteroid level to 74 mg. per 24 hours and the plasma 17-hydroxycorticosteroid level to 75 µg. per 100 ml.

*Operation* 16.11.53 (Mr. Selwyn Taylor).—Bilateral adrenal hyperplasia was found. The whole of the right adrenal (11·5 grammes) was removed and 5·5 grammes of the left adrenal. During the operation period cortisone, Eucortone and intravenous nor-adrenaline were given.

Ten days after operation the patient appeared less plethoric and had lost 8 lb. in weight. The striæ had faded slightly. The urinary excretion of 17-ketosteroids had fallen to 7 mg. per 24 hours and the plasma 17-hydroxycorticosteroids to 9 µg. The blood-pressure was still raised, 160/100.

At that time it was feared that not enough adrenal tissue had been removed. At follow-up on 25.1.54, however, the blood-pressure was 145/90, the striæ were much faded and there was a considerable amount of brown-black pigmentation in the mouth. The patient looked and felt well, but his sexual potency had not returned.

**Diabetes Insipidus, Obsessional Neurosis and ? Hypothalamic Dysfunction.**—RUSSELL BARTON, M.B. (for BRIAN ACKNER, M.R.C.P.).

Miss I. O., aged 29. Admitted to Westminster Hospital under the care of Dr. Gerald Garmany for three months in March 1952, having been socially and occupationally disabled by obsessional rituals (washing, performing tasks in multiples of 6) and obsessional ruminations (that she smelt badly and was unable to complete performance of tasks satisfactorily) for four months. Excessive thirst and drinking had been present for fifteen years, mild obsessional symptoms for one year, sporadic urinary incontinence for one year. Ideas of reference, subjective hypothermia and transient hypersomnia had been occurring since four months before admission, for no ascertainable cause; coincidentally the obsessional symptoms and polydipsia had worsened.

*Personal history.*—Normal early life, poor scholar, poor work record. No evidence of an encephalitis in childhood. Always shy, sensitive and submissive.

*Family history.*—Father an ill-tempered, moody and formerly alcoholic Irishman, whose sister died in a mental hospital (untraced).

*Investigations* revealed: (1) Low average I.Q. (Wechsler Bellevue 82); (2) Diabetes insipidus, responding to Pitressin (Fig. 1); (3) Hyperglycæmic blood sugar curve; (4) Abnormal bladder capacity (3½ pints); (5) Diminished micturition reflex (40 cm. $H_2O$) (Fig. 2), and (6) Dysdiadochokinesis of the left arm, which swings less on walking. Other investigations, in which no abnormality was found, included C.S.F., blood counts, serum cholesterol, serum calcium, W.R., Kahn, renal function tests and urinary ketosteroid excretion. X-rays of skull, skeleton and lung fields, barium meal, air encephalogram, and perimetry revealed nothing abnormal.

Following administration of aqueous Pitressin 0·75 c.c. i.m. b.d. and supportive psychotherapy, drinking diminished, rituals reduced, and ruminations receded but remained marginally conscious. Patient was discharged in July 1952, and remained improved until early 1953 when symptoms worsened, patient became depressed, dishevelled, and unwilling to go out.

Admission to the Maudsley Hospital under the care of Dr. Brian Ackner was arranged by Dr. Gerald Garmany, in June 1953, with a view to leucotomy. A history consistent with the foregoing

was obtained and investigations yielding normal results included E.E.G., A.E.G., adrenaline sensitivity test. Abnormal results were Hb 67% (normocytic anæmia), and diuresis not responding to 2·5% saline infusion (Carter and Robbins, 1947). Psychological tests revealed conflicting evidence for brain damage. Pitressin was continued, 0·75 c.c. i.m. b.d., but patient failed to improve and rituals, ruminations, almost constant depression and anxiety have persisted.

This case had been examined by several general physicians, all of whom had failed to discover the obsessional symptoms, and it was apparent that diabetes insipidus accompanied by obsessional symptoms might be encountered by general physicians, who may fail to remark on the psychiatric aspects of the syndrome.

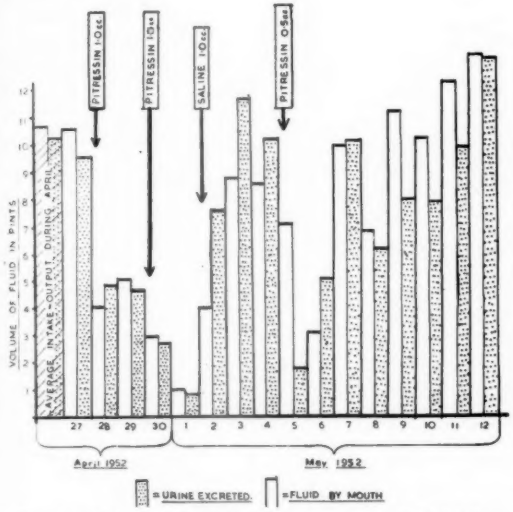



FIG. 1.—Effect of i.m. Pitressin Tannate on fluid intake and urinary exertion.

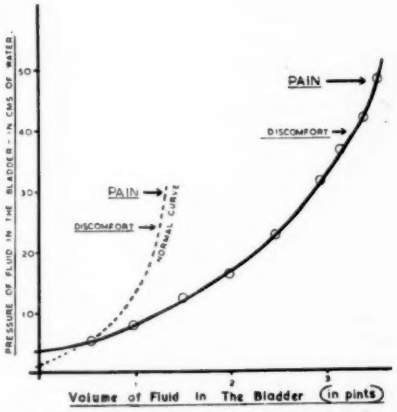



FIG. 2.—Miss I. O., aged 28. Cystometry July 2, 1952 (Jessiman and Barton).

There is a similar case in the Maudsley Hospital at present—a long-standing obsessional illness following encephalitis when the patient was aged 13, in which diabetes insipidus appeared five years after the onset of the mental disturbance. Obsessional illness is well recognized as a sequel to encephalitis lethargica as is diabetes insipidus. The occurrence of both in the same patient is not well documented, although the structural and functional implications of such a syndrome are most interesting. McCowan and Cook (1928) reported a case of a woman aged 33 suffering from post-encephalitic Parkinsonism, with a polydipsia which they suggested was probably obsessional.

It is interesting to note that the present patient has a cluster of symptoms which could be predicted, from experimental work, to follow impairment of function of structures in the hypothalamic area. The obsessional symptoms would appear to be an exception—they have been recorded in post-encephalitic cases in which the lesion has subsequently been found to be predominantly located in the region of the mid-brain, usually involving only the most caudal part of the hypothalamus.

Although the abnormal bladder capacity and raised pressure threshold required to initiate micturition is usually attributed to the bladder becoming used to storing large volumes of urine in cases of diabetes insipidus, it seems justifiable to offer another explanation—that there is a dysfunction in the pre-optic region of the anterior hypothalamus, stimulation in which area has been observed to cause paroxysmal bladder contraction (Beattie and Kerr, 1936; Ranson *et al.*, 1935). As well as having an abnormal bladder capacity, this patient has been incontinent of urine, on one occasion shortly after having emptied her bladder.

## REFERENCES

BEATTIE, J., and KERR, A. S. (1936) *Brain*, **59**, 313.
CARTER, A. C., and ROBBINS, J. (1947) *J. clin. Endocrin.*, **7**, 752.
MCCOWAN, P. K., and COOK, L. C. (1928) *Lancet*, i, 1316.
RANSON, S. W., KABAT, H., and MAGOUN, H. W. (1935) *Arch. Neurol. Psychiat., Chicago*, **33**, 469.

**Cushing's Syndrome. Removal of Adrenocortical Adenoma. Subsequent Adrenal Hypofunction.**—A. STUART MASON, M.D.

Female, aged 39.

First admission April 1951. Two years gain in weight. One year amenorrhœa. One year increasing weakness of lower limbs and aching pain in chest. Six months hypertension noted.

*On examination.*—Classical facies and habitus of Cushing's syndrome. No livid striæ but purpura and ecchymoses. Considerable wasting and weakness of leg muscles.

C.V.S.: Mitral stenosis. B.P. 170/130 (six months previously 155/95).

X-ray chest: Spontaneous fractures of three ribs.

Glucose tolerance test: Diabetic curve.

Serum calcium 8 mg.%; phosphorus 4·6 mg.%.

17-ketosteroids: 24-hour output varying from 7 to 10 mg.

I.V.P.: Left kidney displaced downwards. Mass visible in left suprarenal area.

16.5.51: Removal of left adrenocortical adenoma by Professor V. W. Dix. Period of operation covered by i.m. cortisone therapy.

Cortisone continued at 50 mg. daily to 22.5.51. ACTH given 20.5.51–28.5.51.

Patient's blood pressure returned to normal within twenty-four hours of operation and signs of Cushing's syndrome rapidly diminished. General condition remained good until:

26.5.51: Onset of anorexia, lethargy, muscular weakness and pain in back. These symptoms persisted and became more severe associated with hypotension, rising serum potassium and falling serum sodium. 17-ketosteroids = 2 mg./24 hours.

1.6.51: Cortisone recommenced (100 mg. daily) with dramatic clinical effect. Treatment continued until 19.6.51.

4.6.51–3.7.51 ACTH given.

23.6.51: Symptoms similar to first collapse recurred. Again, relief with further cortisone. Both these attacks occurred after stopping cortisone but when ACTH was still being administered.

Cortisone was continued in small dosage until her discharge on 13.9.51.

From 1.8.51–7.8.51 ACTH given with no evidence of adrenal response.

28.9.51: Readmitted in Addisonian crisis. Dramatic response to cortisone and salt. Symptoms began to recur when DOCA substituted for cortisone. Patient then restabilized on cortisone 50 mg. daily. ACTH given for one week produced no adrenal response.

Continued cortisone as an out-patient and remained in relatively good health until:

11.6.52: Readmitted for assessment. Cortisone stopped for fourteen days. Repeated 17-ketosteroid estimations—average 24-hour output 2·5 mg. Marked hypoglycæmic unresponsiveness. B.P. 155/60.

Course of ACTH given which led to severe allergic reaction which in turn precipitated minor Addisonian crisis, successfully relieved by cortisone. Discharged to continue cortisone.

1.11.52–8.11.52: Readmitted with acute pyelitis. Treated with extra cortisone. Then given implant of 400 mg. testosterone. This led to increased muscular strength and considerable salt retention.

The patient has continued in fair health on a maintenance dose of oral cortisone 50–75 mg. daily until the present. She has little resistance to fatigue and is incapable of severe effort. She is now readmitted for assessment. At present (November 1953) (still on cortisone) B.P. 100/60, serum sodium 300 mg.%, potassium normal. Kepler index = 7. 17-ketosteroids, 3·7 mg./24 hours.

*Comment.*—The main point for consideration in this case is the prolonged adrenal insufficiency following removal of a functioning adrenocortical adenoma. Cortisone was undoubtedly life-saving in the first post-operative weeks and has been a necessity of treatment ever since.

ACTH has been given for considerable periods of time with no apparent adrenal response. Administration of ACTH has been complicated by the occurrence of allergic reactions. Throughout she had been given Armour's (pig) ACTH.

Either she has no adrenocortical tissue on the right side or the atrophy which occurred during her Cushing's syndrome has not responded to the stimulus of ACTH. Natural recovery of adrenal function has been prevented by the necessity of administering cortisone.

She is now in hospital for a prolonged trial of Crookes' (beef) ACTH. It is hoped that this preparation might not lead to allergic reactions. In the treatment of such atrophic adrenals the interesting point arises whether the ACTH given should be potent in ascorbic acid depleting properties or in adrenal weight-maintaining properties.

POSTSCRIPT (March 1954).—The patient has had no allergic reactions to beef ACTH. There was a significant fall in eosinophils following its administration. The Kepler index returned to normal but there has been little rise in 17-ketosteroid excretion. Clinically she has remained in fair health to date on continual ACTH therapy. It is concluded that an adrenal is present which is responding slowly to ACTH.—A. S. M.

**Myelosclerosis. Diabetes Insipidus.**—OLIVER GARROD, M.D.

J. M., retired Army Officer, aged 47.

*History.*—Illness dates from December 1946 when he felt "run down". Blood count showed hæmoglobin 88%, R.B.C. 4,000,000, red cell fragility normal, 7 erythroblasts and normoblasts per 200 W.B.C.

February 1947: Spleen 2 fingerbreadths enlarged. Sternal marrow showed "erythroblastic response".

April 1949: Tingling in legs, otherwise well. Spleen 4 fingerbreadths and liver 2 fingerbreadths enlarged. No icterus but serum bilirubin 4 mg.%. Hæmoglobin 11·8 grammes %. W.B.C. 8,100 (myelocyte series 6%). Reticulocytes 12%. Sternal marrow unchanged. Acholuric jaundice was diagnosed and splenectomy performed in January 1950.

February 1951: Admitted to Hammersmith Hospital (Dr. Sheila Sherlock). Myelosclerosis was diagnosed on the basis of: (1) Leuco-erythroblastic blood picture. (W.B.C. 34,000, myelocyte series 4%, nucleated R.B.C. 15 per 100 W.B.C.) (2) Iliac crest biopsy (Scanty hæmopoiesis, marrow spaces fibrosed). (3) Liver biopsy (myeloid metaplasia). (4) Bone X-rays (patchy sclerosis of pelvis and femora).

He remained well apart from melæna (1950, 1951) and epistaxes (1953), until August 1953 when sudden onset of severe polydipsia and polyuria only relieved by Pitressin snuff. Urine: specific gravity 1001 to 1003; no albuminuria or glycosuria. Blood urea 36 mg.%.

X-rays: Skull base shows increased bone density but no enlargement or bridging of sella turcica. Femora show gross cortical thickening. Hæmoglobin 115%, W.B.C. 80,000 (myelocyte series 24%).

October 1953: Diabetes insipidus (neurohypophyseal lesion) confirmed by the following tests:

(1) *Twenty-four hour fluid deprivation.*—Weight loss 4·1 kg. Urine loss 5·5 litres. Maximum urine sp. gr. 1008.

(2) *Intravenous nicotine test* (patient a non-smoker).—1 mg. of nicotine base intravenously caused no antidiuresis. 2 mg. caused minimal antidiuresis (urine flow fell from 10·1 to 5·3 ml./per minute, and sp. gr. rose from 1003 to 1007).

Antidiuretic response to intravenous Pitressin was normal.

*Conclusion.*—The diabetes insipidus is thought to be due to pressure on the hypothalamus or the pituitary stalk from either thickened bone or a focus of myeloid metaplasia.

**Exophthalmic Ophthalmoplegia Supervening on Spontaneous Myxœdema.**—I. C. GILLILAND, M.D., M.R.C.P.

Mrs. D. C., aged 52, housewife.

*Past history.*—The patient says she always had prominent eyes. In 1934 she had her first child, and had much domestic stress and many nervous episodes since 1939 when, attending her doctor for other matters, he noticed her prominent eyes and fast pulse, and put her on Lugol's iodine, five drops, t.d.s., which she continued to take, with one small intermission, until first seen in 1951.

*Recent history.*—She presented in 1951 suffering from cold hands with "pins and needles". On examination, she had a typical myxœdematous appearance, scaly dry skin, dry hair, husky voice. She had right eyelid retraction at this time. The myxœdema was confirmed by $I^{131}$ test (T 1·4), cholesterol 400 mg.% and characteristic ECG tracing.

She commenced l-thyroxine therapy with 0·1 mg./day, on which her symptoms and feeling of cold improved. After nine months on this dose she first complained of diplopia on upward and lateral movement. The dose was increased to 0·2 mg. daily. She developed proptosis especially on the left, and diplopia above the horizontal position. Her upward eye movements were limited to 42 degrees on the left and 38 degrees on the right (Fig. 2, 17.6.52). A prostigmine test at this time showed no improvement. The dose was increased to 0·6 mg. daily. After one month on this dose her spontaneous complaint of diplopia was less, but her eyes were still prominent and movements were 38 degrees on the right and 50 degrees on the left in an upward direction. Her B.M.R. at this time was +26%. After six months she was reassessed. There was lid bulge and proptosis in both eyes (Fig. 1). Ocular movements were measured (Fig. 2, 12.9.53).

For one month before the demonstration she had been off thyroxine. The myxœdema has been confirmed: $I^{131}$, T 1·7: cholesterol 300 mg.%: ECG typical of myxœdema. Proptosis appears unchanged but eye movements are more restricted (Fig. 2, 22.11.53) and diplopia occurs on looking straight ahead as well as laterally. Thyroxine therapy has recommenced with subjective improvement in diplopia.

*Discussion.*—It seems reasonable to infer that this patient suffered from Graves' disease in her earlier life, and that the Lugol's iodine which she took for many years was prescribed on this diagnosis. She herself did not feel she suffered from any illness at this time, nor did she appreciate any benefit from the medication.

FIG. 1.—Lateral view showing proptosis.

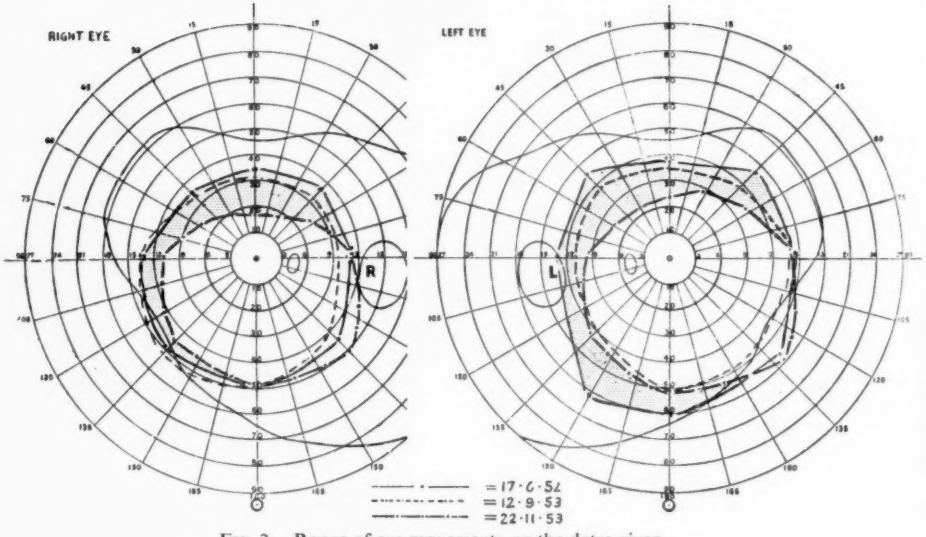



FIG. 2.—Range of eye movements on the dates given.

When first seen twelve years later, she had developed spontaneous myxœdema, classical in appearance and confirmed by B.M.R., cholesterol, ECG and $I^{131}$ tests.

The main interest arises from the fact that she developed symptoms of diplopia and signs of proptosis and ophthalmoplegia in the course of the treatment of her myxœdema. These did not improve on full therapy doses of thyroxine, but worsened when she was allowed, for a short period, to become myxœdematous again. She is now under further treatment for her myxœdema but it is too early to say whether there has been any change.

POSTSCRIPT (March 1954).—On further treatment the situation is now the same as when she was on full doses of thyroxine previously.—I. C. G.

# Section of Neurology

President—MACDONALD CRITCHLEY, M.D., F.R.C.P.

[*September* 1, 1953, *contd.*]

JOINT MEETING WITH THE CANADIAN NEUROLOGICAL SOCIETY
AFTERNOON SESSION

Chairman—H. H. HYLAND, M.D., F.R.C.P.(Lond.), F.R.C.P.(Can.)
(President of the Canadian Neurological Society)

## Pain in Paraplegia

### Clinical Management and Surgical Treatment

By E. H. BOTTERELL, M.D., F.R.C.C., J. C. CALLAGHAN, M.D., A. T. JOUSSE, M.D.
*Toronto, Ontario, Canada*

DIMINISHED or absent sensation below the level of the lesion is a conspicuous feature following spinal cord injury. Of equal importance is the frequent occurrence of pain referred to the portion of the body rendered anæsthetic.

The nature and severity of the pain is assessed by the patient in relation to his past experience, emotional stability, intelligence and state of well-being. Severe pain is successfully endured by certain patients and they are able to live useful lives, while others are unable to cope with the problem. A few suffer so severely that surgical treatment is required if survival and rehabilitation are to be made possible.

In this study pain is evaluated in terms of severity, quality, location and incidence; aggravating and alleviating factors are discussed; the means whereby pain is produced are considered. The total reaction of the patient to suffering is described. The results of surgical treatment are assessed.

#### METHOD OF COLLECTING INFORMATION

A study has been made of 125 patients suffering from traumatic paraplegia who were treated in the Department of Veterans Affairs Neurosurgical Unit at Christie Street and Sunnybrook Hospitals and Lyndhurst Lodge in Toronto, Canada. Although the patients were well known to the authors, each answered a questionnaire regarding pain. 34 patients were interviewed personally in order to check on the validity of the questionnaire.

#### ASSESSMENT OF PAIN

To a degree, assessment of the quantity or severity of pain depends upon the patient's capacity to describe his discomfort. However, certain signs of severe suffering are known, and these have been vividly described by Weir Mitchell *et al.* (1864), in patients with causalgia: "As pain increases the temper changes and grows irritable, the face becomes anxious and has a look of weariness and

suffering. The sleep is restless. . . ." In our experience, patients with severe pain may wince, writhe or cry out. Interference with sleep and appetite leads to emaciation and the patient becomes gaunt and hollow-eyed. He becomes a solitary type of person, unable to participate in diversional or vocational activities. He is a problem to the attending staff. to himself and his friends and family.

The above observations relate to those who suffer severe pain over a protracted period so that the resources of fortitude possessed by the patient are overwhelmed. Paraplegic patients with pain of such severity require surgical treatment if retraining and rehabilitation are to be achieved.

The evaluation of pain qualitatively is more difficult. The patient who may not be articulate is faced with the necessity of describing a sensation, or series of sensations, of which he may never have experienced a counterpart. In addition, he is attempting to convey his experience to someone who has, in all likelihood, never suffered pain more severe than a mild toothache. There is, in fact, very little relevant experience which is common to the sufferer and to those who have no pain. It is like attempting to describe colours to one who has been born blind. This is most clearly portrayed when one cross-questions the patient and tries to make him state precisely the type of discomfort he experiences.

Patients who suffer most severely describe their pain as "sharp", "a dull ache", or "vice-like". This is commonly superimposed on a background of burning pain. Numbness and tingling do not constitute a very severe form of discomfort. About half the patients feel that muscle spasms aggravate pain, though many who made this observation did not suffer from visible muscle spasms. Presumably these patients experience a sensation akin to the feeling one has when there is a muscle spasm or cramp in the leg.

The same descriptive terms were used by patients with partial or complete cervical, thoracic and cauda equina lesions. Similarly, the quality of the pain is not helpful in differentiating root pain from pain of central origin, for the patient uses the same descriptive words irrespective of the nerve structures involved.

The observations of Lewis and Hess (1933) support the view that pain is difficult to evaluate qualitatively. They point out that skin pains may be described by patients as "pricking", "tearing", "stinging" or burning". They emphasize that these terms give inadequate definition, for they refer to the agent which caused or might have caused the pain. In addition, the quality of the pain may be altered in character by varying the duration of the stimulus, whereas it is not dependent on the mechanism of stimulation as was shown by using an electric current, a pinch, a tug on a single hair, or a hot wire as stimuli. If the duration is short, a pricking sensation is reported, and, if prolonged, burning is described. There is never any doubt in the subject's mind but that the pain derives from the skin, and it may be readily localized (Lewis, 1942).

Wolff and Wolf (1948) emphasize that pain originating in deep structures is distinctive and is easily differentiated from superficial pain, for it is more diffuse, cannot be well localized and is continuous. The patient may describe it as "aching", "boring", "vice-like" or sharp". It is sickening and he reacts by perspiring, becoming nauseated and vomiting. Thunberg (1902) describes this pain of deep origin as being "dull". Whether produced by pressure, injection of hypertonic solutions or fatigue in a muscle, the quality does not vary.

## Referral of Pain of Central Origin

The pain in paraplegia is referred to the dermatome corresponding to the injured segment of cord or the anæsthetic area below it, and is described by the patient on the basis of past experience of pain. For the purpose of definition, the body was divided into the areas shown in Table I.

Table I.—Location of Pain of Central Origin

| | Torso | Viscera | Perineum | Arm | Forearm | Hand | Thigh | Leg | Foot |
|---|---|---|---|---|---|---|---|---|---|
| Cervical (partial) 14 cases .. | 8 | 0 | 1 | 5 | 6 | 5 | 8 | 7 | 6 |
| Cervical (complete) 6 cases .. | 3 | 1 | 0 | 0 | 0 | 3 | 1 | 2 | 2 |
| Thoracic (partial) 11 cases .. | 6 | 1 | 0 | 1 | 1 | 1 | 5 | 7 | 5 |
| Thoracic (complete) 59 cases | 36 | 2 | 0 | 0 | 0 | 0 | 34 | 29 | 30 |
| Cauda (partial) 25 cases .. | 9 | 4 | 3 | 0 | 0 | 0 | 19 | 19 | 18 |
| Cauda (complete) 10 cases .. | 1 | 1 | 0 | 0 | 0 | 0 | 8 | 3 | 4 |

For each level of lesion one or more patients reported pain referred to all the regions designated, save that perineal pain was absent in 70 cases of injury to the thoracic cord and was rarely reported by the other patients. This may be due to the inability of the patient to localize this anatomical area. Similarly, pain was rarely described as occurring within the abdomen but when present the phrases "abdominal cramps" or "burning in the bladder" were used. Lewis (1942) has pointed out that it is not always possible to differentiate between visceral pain and that which arises from (or is referred to) deep somatic structures such as bone, tendon or muscle.

### Incidence and Severity of Pain

The incidence of pain in paraplegia is high. Of 125 cases assessed (Fig. 1), 118 (94%) reported pain or discomfort. However, less than one-third of the whole group found pain of troublesome severity, and but 9 patients experienced intolerable pain requiring surgical intervention.

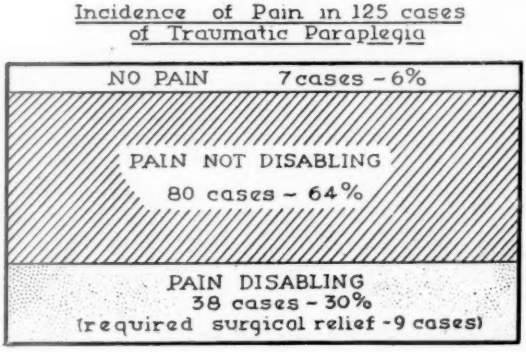

Incidence of Pain in 125 cases
of Traumatic Paraplegia
NO PAIN 7 cases - 6%
PAIN NOT DISABLING
80 cases - 64%
PAIN DISABLING
38 cases - 30%
(required surgical relief - 9 cases)

Fig. 1.

Probably some of the more stalwart patients refused to admit that their pain was disabling, whilst others with less fortitude succumbed to a lesser degree of pain, suggesting that a small number from the two lower sections of Fig. 1 might be interchanged.

Of the 38 patients who found pain of troublesome severity, 29 were able to gain personal independence and leave hospital, although suffering with such severity as to interfere at times with sleep and appetite as well as with vocational and diversional activities. Some members of this group may yet require surgical treatment. The following case report deals with one such patient:

*Case I.*—C. M.—A perforating gunshot wound of the spinal cord produced a clinically complete flaccid paralysis below the tenth thoracic segment. Sharp, burning pain in the lower extremities has been present intermittently since four months after the injury. The severity of the pain is such that the patient must suspend all activities during an attack which lasts about thirty seconds. At time he writhes with pain. Between these episodes he is free from severe pain and the attacks occur only every two or three hours. Despite the pain he has established a prospering business.

The incidence of severe pain is low in cervical injuries. There is a higher incidence in thoracic and complete conus and cauda lesions, and it is most common following partial destruction of the cauda equina and conus medullaris (Table II).

Table II.—Incidence of Severe Pain in Traumatic Paraplegia

| Level | Cervical | | Thoracic | | Cauda equina | | |
|---|---|---|---|---|---|---|---|
| Type of lesion | Total | Partial | Total | Partial | Total | Partial | Total |
| Cases | 6 | 14 | 59 | 11 | 10 | 25 | 125 |
| Severe pain | 1 | 2 | 14 | 3 | 4 | 14 | 38 |

### Time of Onset of Pain

Our study reveals that patients may suffer severe pain at the moment of injury or as soon as consciousness is regained, and are never free of pain thereafter. On the other hand, the onset of pain may be delayed for years. As a consequence, those patients who are at present pain-free, may yet develop central pain (Table III).

Table III.—Time of Onset of Pain

| Time elapsed from injury to onset of pain | No. of cases | Per cent |
|---|---|---|
| Immediate | 39 | 31 |
| Days or weeks | 24 | 19 |
| Months | 33 | 26 |
| Years | 12 | 10 |
| No pain as yet | 7 | 6 |
| No reply to this question | 10 | 8 |

### Factors which Influence Pain

A state of well-being decreases the impact of pain on the individual. Conditions which undermine the state of health, as do urinary sepsis or infected pressure sores, magnify the patient's reaction to pain. Suffering is more acute in patients depressed by marital or domestic complications and by physical problems, such as bowel and bladder incontinence.

Certain local conditions which enhance pain are of particular interest. Distension of the bladder by excessive residual urine, bladder spasms resulting from uncontrolled infection or calculi, and constipation producing distension of the large bowel, were pre-eminent. Indeed, our clinical experience indicates that aggravation of central pain may precede other clinical signs of an exacerbation of genito-urinary sepsis, or may be an indication of impaction of fæces. No satisfactory hypothesis to account for this observation has been formulated. Aggravation of pain has occurred independent of reflex hyperextension with headache and sweating (Kendrick *et al.*, 1953).

The following case provides an illustration of the relationship between bowel distension and pain in a case of verified transection of the cord above the fifth thoracic segment.

*Case II.*—V. B. *Transection of cord and section of posterior nerve roots.* Gunshot wound of the thoracic spine in April 1945 produced complete sensory and motor paralysis below T–5. Girdle pain at the level of the lesion caused great distress. On March 15, 1946, exploration at the site of the lesion permitted excision of the injured portion of the cord up to and including the lower end of grossly normal cord. The fourth and fifth posterior thoracic nerve roots were divided. At the present time this man describes a burning sensation in his feet. This burning sensation is more marked when the bowel is distended with gas and fæces. He recognizes distension as the abdomen becomes more prominent, his appetite is impaired, and he may experience nausea. A satisfactory bowel evacuation relieves the nausea, restores appetite, and the burning in the feet becomes less severe.

28% of patients reported increased pain with bladder distension. Constipation causing bowel distension increased the pain according to 34% of patients. The mechanism in the 2 cases is no doubt similar, and the response does not vary as between partial and complete lesions.

Many patients report that their pain is made worse by damp cold weather. 14% volunteered this information, although the questionnaire did not include the question. Two patients with cauda equina lesions were transferred to a drier climate and some relief was reported. The relief was quite marked for one man, and could be reversed by a return to a damper climate. 13 patients complained that smoking a cigarette aggravated the pain, and a few stopped smoking in order that they might escape this added suffering.

Where sensation is impaired but not abolished, or where hyperæsthesia exists, stimuli known to be pain producing in normal individuals may accentuate pain.

### Alleviation of Pain

Patients who are able to bear severe pain successfully, frequently report substantial relief from mild analgesics such as aspirin, phenacetin and occasionally codeine. At first this was taken as an indication that the pain was not severe, or its severity was being exaggerated. However, long association with these casualties leads us to conclude that mild analgesics may relieve the most severe phases of the pain, thus rendering that which persists endurable. 24 patients reported significant relief from the mild analgesics. Patients with severe pain have not been given narcotics unless they were terminally ill. The few who were addicted when they came to our service, were broken of the habit by immediate withdrawal. At the same time a programme for rehabilitation was presented to them.

We have found that once the patient grasps the objective of independent life outside a hospital and begins to make progress in the practical measures leading to this goal, slight and moderate degrees of pain of central origin, formerly demoralizing, commonly become tolerable. Apart from the general measures of good nursing and careful urological supervision, we do not believe that severe pain diminishes spontaneously with the passage of time, for we have observed patients who suffered unabatedly for eight years.

### Surgical Treatment of Pain

Among the group of 125 patients with paraplegia of traumatic origin, surgical treatment of pain became necessary in 9 (Cases II–X). In each instance the patient presented a picture of severe suffering and either was unable to make a start toward the goal of rehabilitation or, having achieved independent life at home, was forced by pain to return to hospital. There were 6 cases treated by bilateral spinothalamic tractotomy, one by transection of the cord with section of roots bound by scar tissue, and one by bilateral prefrontal lobotomy. Unilateral spinothalamic tractotomy was done three times in the remaining case.

There follows a short report of each case treated surgically. The final clinical assessment of these patients was made from two to eight years after operation.

*Case II.*—V. B.—*See above.*

*Comment.*—Root pain relieved, burning pain persists in feet. Result good.

*Case III.*—W. R. O. *Bilateral spinothalamic tractotomy.* G.S.W. of the cauda equina in 1944 produced partial paraplegia. Immediate onset of severe burning and stabbing pain in the legs, buttocks and perineum persisted with such marked hyperæsthesia that nursing the patient was a great problem, and irrigation of the bladder was intolerable. Complicating factors were osteomyelitis of the lumbar spine and subphrenic abscess drained on several occasions. The pain was unremitting and the patient's course was steadily downward. Narcotics had added their demoralizing effect. A bilateral spinothalamic tractotomy at the level of the third thoracic vertebra provided analgesia to T–10, and brought dramatic relief, and eight years after operation the relief from severe pain persists with no change in the level of analgesia.

*Comment.*—An excellent result with low level of analgesia.

*Case IV.*—R. G. B. *Bilateral spinothalamic tractotomy.* A fracture dislocation of L–1 on June 29, 1942, produced complete paraplegia. In April 1944, sharp crampy pain in the left groin and pins and needles in the left leg and to a lesser degree in the right leg, were noted. Thereafter pain became severe, interfering with sleep, appetite, and producing depression of spirits. Pain tract section on November 2, 1945, at the fifth thoracic vertebral level raised the level of analgesia to T–10, and temporarily relieved the pain. However, he still complained of burning pain referred to the legs, perineum and external genitalia, and was largely incapacitated by pain five years after operation.

Re-operation was done in November 1951, at the second thoracic vertebral level. Analgesia to T–4 was produced. Two years after operation with the level of analgesia sustained at T–4, the patient reports relief from the burning pain in the perineum, external genitalia and bladder region, but the pain in the legs persists.

*Comment.*—A good result followed the second operation.

*Case V.*—A. J. H. *Bilateral spinothalamic tractotomy.* On August 9, 1944, an exploding shell destroyed the left leg and produced cerebral contusion and spinal cord damage such that the patient was dysphasic and disorientated for months. A complete flaccid paraplegia persisted below L–1 segment. There was no fracture or dislocation of the spine. Two months after injury he first described pain resembling a "spade in the rectum". This persisted intermittently until his death on June 4, 1949. It was aggravated by sitting erect, and partial relief was obtained by lying in bed. A right nephrectomy because of pyelonephritis and calculi, October 31, 1945, did not influence the pain. Spinal anæsthesia extending 6 segments above the lesion did not produce even temporary relief. A bilateral pain tract section on February 22, 1946, at the fifth thoracic vertebral level, raised the level of analgesia to pin-prick to the eighth thoracic segment. No significant relief was obtained and he continued to suffer pain in the rectum until he died of G.-U. sepsis.

*Comment.*—This pain was totally uninfluenced by tractotomy.

*Case 6.*—D. Y. M. *Bilateral spinothalamic tractotomy.* On August 15, 1943, a bullet shattered the first lumbar vertebra and produced complete paraplegia at T–10. Severe pain was present in the back and legs from the moment of being wounded. The pain was described as aching, gripping, burning and stabbing. It varied in intensity from time to time, being aggravated by some atmospheric conditions and ameliorated by others. Smoking maae the pain worse.

A right nephrectomy for pyelonephritis on April 19, 1945, led to improved general health, but did not relieve the pain.

Bilateral pain tract section on May 10, 1946, at T–4 vertebral level, abolished the aching and gripping and stabbing pain, but the burning sensation persisted. However, he was made comfortable and gained many pounds in weight. Anæsthesia to pin-prick was raised to T–6.

*Comment.*—It is noteworthy that burning persisted after spinothalamic tractotomy and with analgesia persisting to T–6.

*Case VII.*—J. C. *Bilateral spinothalamic tractotomy.* On August 19, 1942, a G.S.W. produced complete paraplegia below T–10 segment. Two weeks following injury pain developed in the legs and became progressively more severe. It was described as resembling the thawing out of frozen limbs, and superimposed were sharp crampy pains in the abdomen and thighs. The painful component referred to the right lower quadrant of the abdomen was a sharp, crampy pain, severe and episodal.

Although living at home and bearing heavy administration responsibilities capably, he was underweight and his sleep and appetite were impaired. Pain tract section December 17, 1947, at T–12 vertebral level, abolished the abdominal pain, but the "thawing" type of discomfort persisted. Analgesia to pin-prick was established to the seventh thoracic dermatome bilaterally. The patient gained weight and slept well.

*Comment.*—In eight years since tractotomy the level of analgesia has fallen with considerable return of severe pain. He has regained the capacity to differentiate sharp from dull to some degree from T–6 to T–10, the level of the initial paraplegia.

*Case VIII.*—E. O. B. *Bilateral spinothalamic tractotomy.* G.S.W. on August 29, 1944, produced complete paraplegia below T–11 dermatome. After three weeks pain developed in the back and legs. The patient had the gaunt fatigued appearance of severe suffering and was underweight. Sleep was disturbed. Genito-urinary sepsis necessitated the surgical removal of both testicles. Twelve months later he developed a depression which had the appearance of involutional melancholia. Bilateral tractotomy at T–1–2 vertebral level relieved pain, his depression cleared and he gained 31 lb. in a year. The present level of analgesia to pin-prick three years after operation, is at T–10, one segment above the level of paraplegia.

*Comment.*—An excellent therapeutic result in spite of a low level of analgesia.

*Case IX.*—J. J. A. *Unilateral tractotomy.* On June 14, 1944, a bullet partially destroyed the cauda equina. There was immediate severe pain in the back with sensory loss below L–3 dermatome on the right and L–5 on the left. Pain soon developed in the legs and feet and there was marked hyperæsthesia of the right thigh. The most severe pain was referred to the right thigh, right foot and left foot. The patient became demoralized by pain. On July 7, 1946, unilateral (left) pain tract section raised the level of anæsthesia to the eleventh thoracic dermatome on the right. The pain in the right foot was abolished but the pain referred to the right thigh persisted and the patient was not improved. The operation was repeated September 28, 1946, without much benefit. The patient lived out of hospital with his wife and family, but became a solitary type of man who could

not forget his pain. Consequently, in September of 1951, re-operation was carried out and the left spinothalamic tract again sectioned. Following operation the patient reports pain unabated. The level of analgesia is at T 6, and has remained at this level since operation.

*Comment.*—He remains partially incapacitated by pain but lives out of hospital. It is probable that he would have benefited from a bilateral tractotomy. Ray and Wolff (1945) refer to the case of an individual who, having undergone a unilateral spinothalamic tractotomy at T–1, experienced pain on the side of normal sensation when intense noxious stimulation was applied to the analgesic half of the body.

*Case X.*—R. K. G. R. *Bilateral prefrontal lobotomy.* A clinically complete cervical cord lesion at C–6 resulted from diving into shallow water. The patient early complained of intense burning pain in the legs, lower abdomen and chest. In addition, excessive reflex sweating and headache related to bladder spasms, caused the patient much distress. A subarachnoid alcohol injection relieved the autonomic responses to bladder spasm and troublesome reflex movement of the legs, but not the burning pain. The patient became depressed and irritable, demanded and received sedatives, and was a constant problem to the staff. A bilateral prefrontal lobotomy was carried out on March 4, 1949. Over a period of a few weeks the patient became relaxed and his humour changed; his need for sedation became less urgent. He continues to experience the burning pain in his legs and abdomen but does not complain unless questioned directly. He co-operates well with ward routine and is very cheerful and mixes well with people.

*Comment.*—Excellent result five years after operation.

## Discussion

*Bilateral spinothalamic tractotomy.*—Frazier (1920) in his first paper on spinothalamic tractotomy for intractable pain, reported 6 cases, of which 2 were gunshot wounds of the spine with paraplegia, and the third a gunshot wound involving the sciatic nerve. In each instance relief of pain was achieved, but no report of follow-up studies is included. We have been unable to find among the many papers concerning spinothalamic tractotomy or paraplegia, any report of a long-term evaluation of the welfare of patients who have had bilateral spinothalamic tractotomy. Survival of patients operated upon for intractable pain due to malignancy is commonly measured in months, and before World War II the life expectancy of a paraplegic patient was usually of the same order. The decade following World War II has presented the first opportunity to study a group of paraplegic patients with intractable pain over a period of years following bilateral spinothalamic tractotomy. The results are summarized in Table IV.

Table IV.—Surgical Treatment of Pain
*Bilateral Spinothalamic Tractotomy*

| Patient | W. R. O. | R. G. B. | A. J. H. | D. Y. M. | J. C. | E. O. B. |
|---|---|---|---|---|---|---|
| Segmental level of injury | L2–3 | L–1 | L–1 | T–10 | T–10 | T–11 |
| Type of injury | Partial | Complete | Complete | Complete | Complete | Complete |
| Tractotomy level | T–3 | T–2 | T–5 | T–4 | T–1 | T–1 |
| date | 24.10.45 | 5.11.51 | 22.2.45 | 5.10.46 | 17.12.47 | 23.5.50 |
| Injury to tractotomy | 15 months | 100 months | 18 months | 33 months | 64 months | 68 months |
| Analgesia post-operatively | T–10 | T–4 | T–8 | T–6 | T–7 | T–10 |
| Analgesia raised | 4 segments | 9 segments | 5 segments | 4 segments | 7 segments | 1 segments |
| Immediate results | Excellent | Good | Poor | Excellent | Excellent | Excellent |
| Present level of analgesia | T–10 | T–4 | Deceased | T–6 | T–10 | T–10 |
| Follow-up | 8 years Excellent | 2 years Good | Deceased | 6½ years Excellent | 5½ years Fair | 3 years Excellent |

In each instance the spinal cord injury was situated between thoracic 10 and lumbar 3 segments—the thoracolumbar region. There was a significant rise in the level of analgesia in all but one patient (E. O. B.) yet he had an excellent result. The term "excellent" describes the result in those patients who show dramatic improvement in appearance, mood and personality. Weight gain was recorded up to 50 lb. in a few months. Restful sleep without analgesia became possible. The term "good" described the result in patients who, while markedly improved, continue to be troubled at times by pain. Fair results are still less favourable, but the patient has less pain than before operation. Case IV (R. G. B.) underwent a second operation, for the first did not produce a sustained high level of analgesia and relief of pain. The results remain good two years after the second operation. The pain was not influenced by operation in Case V (A. J. H.) reported as poor. This patient had suffered injury to both brain and spinal cord. Bilateral spinothalamic tractotomy in 6 cases has produced 3 excellent results which have endured for periods of three, six and eight years—a good result of two years' duration and a fair result at five and a half years, which was excellent for the first two years. This last, Case VII (J. C.), is the only one in which recurrence of pain has occurred as the level of analgesia has slowly fallen.

In retrospect, it seems clear that it would have been preferable to have sectioned the spinothalamic tracts at the level of T-1-2 vertebræ (Freeman and Heimburger, 1947) or at the second cervical vertebra, with a sufficiently generous division of the anterior quadrants of the cord that a persisting high level of analgesia would result (Kahn, 1952). Our follow-up studies indicate that such a high level is not regularly required, but with the fall in the level in Case VII, there has been recurrence

of severe pain, and in Case IV relief was not achieved until a high level of analgesia followed a second operation.

Burning pain has proved a problem difficult of solution in cases of injury to the lumbosacral, thoracic and cervical portions of the spinal cord with either complete or incomplete destruction of cord function. Operation relieved burning pain in 3 of 4 patients in this group of lumbosacral injuries. Burning pain of twenty years' duration and of increasing severity with an incomplete lesion of conus and cauda equina was uninfluenced by bilateral tractotomy at T-1-2 with analgesia to T-4. This case was not one of the patients in the group under consideration. By contrast, jabbing, shooting, crampy, gripping, colicky and vice-like pains, have been regularly relieved by satisfactory bilateral tractotomy. We do not believe unilateral spinothalamic tractotomy has a useful place in the surgical treatment of pain secondary to spinal cord injury. Increased pain or pain of a new quality has not occurred following operation in this series. Pollock has encountered an onslaught of pain, following operation, that had not existed previously (Pollock *et al.*, 1951).

*Prefrontal lobotomy.*—Burning pain was of demoralizing severity following a clinically complete lesion at C-5-6 (Case X). Bilateral prefrontal lobotomy was performed. The ensuing period of five years in a paraplegic unit has provided an unusual opportunity for observation. He has retained the ability for planned thinking, a good sense of humour and concern over the welfare of his family. Uncouth language featured the weeks following operation and, since, when he has had two or more drinks of alcoholic beverage.

## Production of Pain

Pressure on a nerve root by fragments of bone or cartilage or scarring of the meninges, is a known cause of pain. Holmes in 1919, described pain caused by a cervical cord injury and referred to the lower extremities, attributing it to injury of the anterolateral columns of the cord. He judged the lesion to affect the conduction of impulses but not to block the pathway.

Pollock *et al.* (1951) have reported no relief of diffuse burning pain following spinal anæsthesia injected below the lesion and limited in spread by a subarachnoid block, and similar studies on 2 of our cases support this observation. Spread of the anæsthetic agent so the distal injured end of the proximal segment of the cord is anæsthetized, temporarily stopped the pain. They attribute the site of origin of this pain to the distal end of the proximal portion of the cord. One of their patients continued to have the same burning pain following amputation of his leg, eliminating the possibility of centripetal impulses from the amputated limb which can give rise to such sensations.

Davis and Martin (1947) administered tetra-ethyl-ammonium chloride to 30 patients without significantly relieving diffuse burning pain. In our cases a significant observation is the presence of pain, in 2 cases, below the level of clinically complete cervical lesions and in Case II with surgical transection of the cord above T-5. It is difficult to escape the conclusion that pain in complete lesions results from disturbance of function of the central nervous system following the lesion of the spinal cord and independent of peripheral stimuli either interoceptive or exteroceptive, arising below the level of injury.

The hypothesis is put forward that, in certain cases, pain can be explained by escape of thalamic function, due to interruption of ascending spinal pathways with resulting loss of an inhibitory effect of normal afferent impulses. Thalamic function may be disturbed as a secondary effect following upon loss of normal ascending spinal impulses acting upon the reticular formation. Magoun (1950) has demonstrated the importance of the reticular formation of the brain-stem in regulating the background activity of the remainder of the central nervous system. It lies in parallel with long afferent and efferent neural systems, receives connexions from both of them and exerts influences of its own at caudal and cephalic levels. The part played by the reticular formation with regard to pain in humans must be developed in the future.

Holmes' (1919) concept, with which Foerster agreed, of pain arising from an incomplete lesion in the antero-lateral quadrant of the cord, and abnormal function, does, in fact, offer an explanation for certain of our cases. Damage to ascending pathways may result in repetitive stimulation of the pain pathway and activation of a neuronal pool in the reticular connexions or thalamus, with the production of pain. The production of pain following injury of the spinal cord is a problem requiring further physiological study in man.

## Summary and Conclusions

(1) 125 cases of traumatic paraplegia were studied with regards pain. A questionnaire was filled out by each and 34 were interviewed personally. The pain is evaluated in terms of severity, quality, incidence and location. Aggravating and alleviating factors and surgical and non-surgical treatment are discussed. The total reaction of the patient is evaluated.

(2) Pain or discomfort is nearly always experienced in traumatic paraplegia, but it is of disabling severity in less than one-third and requires surgical treatment in less than 10% of cases.

(3) The mode of injury does not influence the severity, quality or incidence of pain.

(4) Disabling pain is relatively uncommon in cervical lesions and is very common in cauda equina injuries. Partial cauda equina injuries show the highest incidence of severe pain.

(5) Successful treatment requires an understanding of the patient's emotional and psychological,

as well as his physical requirements. If these needs are met, the majority of patients learn to live with their pain. Those few who cannot carry on should be relieved by surgical means.

(6) Bilateral spinothalamic tractotomy at the level of the first or second thoracic vertebra or higher, has proved most efficacious in relief of pain. 6 cases are reported with a two to eight year follow-up.

(7) One case of bilateral prefrontal lobotomy is reported, with a five-year follow-up.

BIBLIOGRAPHY


DAVIS, L., and MARTIN, J. (1947) *J. Neurosurg.*, **4**, 483.
FRAZIER, C. H. (1920) *Arch. Neurol. Psychiat., Chicago*, **4**, 137.
FREEMAN, W., and HEIMBURGER, R. (1947) *Arch. Surg. Chicago*, **55**, 433.
HOLMES, G. (1919) Pain of central origin. In: Contributions to medical and biological research, dedicated to Sir William Osler. New York: **1**, 235.
KAHN, E. (1952) *J. Neurosurg.*, **9**, 611.
KENDRICK, W. W., SCOTT, J. W., JOUSSE, A. T., and BOTTERELL, E. H. (1953) *Treatm. Serv. Bull., Ottawa*, **8**, 437.
LEWIS, T. (1942) Pain. New York: pp. 38, 39, 40.
——, and HESS, W. (1933) *Clin. Sci.*, **1**, 39.
MAGOUN, H. W. (1950) *Physiol. Rev.*, **30**, 458.
MITCHELL, S. W., MOREHOUSE, G. R., and KEEN, W. W. (1864) Gunshot Wounds and Other Injuries of Nerves. Philadelphia.
POLLOCK, L. J., *et al.* (1951) *J. Amer. med. Ass.*, **146**, 1551.
RAY, B. S., and WOLFF, H. G. (1945) *Arch. Neurol. Psychiat., Chicago*, **53**, 257.
THUNBERG, T. (1902) *Skand. Arch. Physiol.*, **12**, 394.
WOLFF, H. G., and WOLF, S. (1948) Pain. American Lecture Series, No. 5. Springfield; p. 22.


## Loss of Visualization

By Sir RUSSELL BRAIN, D.M., P.R.C.P.

IN this communication I shall describe 2 patients who, in both cases after a head injury, suffered from a severe degree of inability voluntarily to visualize familiar objects. One patient has been under observation for seventeen years since his head injury, the other died seven years after his. Neither showed any improvement.

This symptom was first described by Charcot (1889). Describing his patient he said: "In every instance the visual memory of forms and colours had completely disappeared, yet he could perceive them when present without difficulty." This patient could not visualize his wife and children nor the home of his youth, and his power to visualize colours was also lost. Charcot added: "It is an interesting detail that in his dreams the patient has no longer the visual representation of objects." Wilbrand (1892) is often credited with reporting another instance, but his patient appears to have suffered from loss of topographical memory rather than from loss of visual imagery for objects.

*Case I.*—Male, a builder's manager, right-handed. In 1936, at the age of 36, he had a car accident which caused a depressed fracture in the mid-frontal region and after which he was unconscious for eight days. His wife was killed in the same accident. When seen for the first time five years after the accident the patient complained that what he called his "picture memory" was gone. He could no longer form a visual image of his first wife nor of his second wife, nor, indeed, of anyone he knew. This did not interfere with recognition. Even if he had only met a man once, although he could not form a mental picture of his face he would recognize him the next time he met him. As a builder's manager he found it a handicap as he could not visualize a plan or an elevation, in consequence of which he had to keep referring to the specifications when dealing with a house. He built his own house by remodelling four cottages and he would work out all the alterations on a plan at night and would then inspect the work next day in order to correct any mistakes he had made in the plan. Similarly if he was going on a journey by car, although he had travelled on the same route before, he would have to look it up afresh on maps and retrace it because he could no longer picture the route, but he was able to recognize landmarks when he came to them. Nevertheless, he was able to describe an object which he could not visualize, for example, his own house. He could not visualize parts of his own body, e.g. his hand. His difficulty in visualizing applied equally to experiences which he had had before the head injury and to subsequent experiences. He continued to dream, but said that since the accident his dreams had been "uncanny". He said: "When I dream I seem to know what is happening, but I don't seem to see a picture. I can dream about a person without seeing them and can remember the person, but not having seen them." He had no difficulty in reading or writing and could remember what he had learned by heart, but found it more difficult than previously to remember what he had written down, because he could not visualize it. He had some difficulty in spelling, which he attributed to the fact that he could not visualize the word. He had, as he put it, "to work it out".

When examined again ten years later, and fifteen years after his head injury, the patient's complaints were unchanged. His only defect in the sphere of speech was a slight degree of verbal

aphasia. There had never been any apraxia or agnosia, nor disturbance of appreciation of external space. The only disorder of the body-schema was his inability to visualize parts of his body. Nevertheless, he could identify spots touched on his body and mark them accurately on a chart. Routine examination of the fundi and central nervous system yielded no evidence of any physical abnormality. His visual fields were full and showed no central scotomas. There was a shelving circular depression ¼ in. in diameter in the mid-frontal region slightly to the left of the middle line. The report on the EEG on 31.5.51 was as follows: "The EEG is abnormal.

"Alpha activity at 11 c/s occurs in the posterior and central areas but is rarely dominant owing to an excess of fast activity at 20–24 c/s and of slow activity mainly at 5–7 c/s. The alpha rhythm is more clearly seen over the right hemisphere than the left. In both hemispheres it is blocked on eye opening. The fast activity occurs symmetrically but the 5–7 c/s waves appear more often on the left, especially frontally.

"On photic stimulation following responses occurred in both parieto-occipital regions though better on the right. With the eyes open and the lamp so placed as to stimulate mainly one half-field following responses were seen in the right hemisphere when stimulated and not in the left; with stimulation applied to the left hemisphere following responses were less clear and were mainly bilateral.

"The asymmetry of alpha activity is within the limits of normal for a right-handed person, but the impairment of response to photic stimulation on the left is possibly indicative of cortical damage."

Dr. O. L. Zangwill and Dr. J. McFie kindly carried out psychometric tests upon this patient with the following results (31.5.51). Tested on items of the Bellevue scale, this man's intelligence was placed in the superior range with I.Q. about 130. Impairment of some tests sensitive to organic deterioration, 14%, was no more than normally expected at his age, and his performance on tests of retention and learning of visual material was adequate. He had some difficulty in verbal learning, and complained of poor memory for names: his spelling was also slightly impaired. Of the Bellevue scale, he did significantly poorly on the picture arrangement test, which is particularly sensitive to frontal lesions.

Dr. Zangwill commented that "there is no doubt that a degree of intellectual loss on formal tests is negligible and, apart from some impairment of spelling, we were unable to elicit any clear-cut signs of organic disability. Despite his complaint of having lost his visual imagery, he is able to deal quite adequately with visual material when asked to describe it from memory. Thus his "memory span" for a number of objects presented in succession is as good as his "memory span" for words or digits. In cases with focal visual retention defects, I have almost always found that immediate memory for a number of visual objects presented in succession is significantly reduced. He is also able to draw designs and describe pictures from memory entirely adequately. Of course one must bear in mind that normal individuals who claim to experience no visual imagery can do this, but cases with defects of visualization usually show some impairment of such tests." Both Dr. McFie and Dr. Zangwill raised the question whether the patient's loss of visualization could be neurotic and a reaction to the emotional stress associated with his accident in which his first wife was killed, but Dr. Zangwill agreed that if a neurotic element could be excluded he thought the case could be accepted as presenting a circumscribed defect of visualization in the absence of other signs of intellectual or memory loss (apart from the very slight dysphasic residua).

*Case II.*—Male, a bank manager, right-handed. In 1945, at the age of 50, he tripped over the entrance to the strong room at his bank and hit his head on a steel cupboard, striking the right fronto-vertical region. He became unconscious, but did not know for how long and recovered consciousness lying on the ground. He was taken home and according to his wife he was not completely conscious for three or four days. He remained in bed for three weeks suffering from headache. When seen nine months after the accident he said "I cannot visualize anything. If I go into a shop or a building, or if I look at a picture, and I want to describe it afterwards I can't see it. If I want to remember what I have been reading I have always visualized the print itself: now I can't do that". He could not visualize his wife's face. He said he could visualize things only "if they come to me as an impression, but I can't make them come". Nevertheless, he never had any difficulty in recognizing either people or objects. He said he could draw a plan of his house, or of the route from the station, but this would involve working it out and would be a slow and difficult process. He said: "I can think of a cucumber or a chair, but I cannot see it. I can't see anything if I shut my eyes". He had experienced no difficulty in speech, reading or writing, but he had noticed some difficulty in adding up columns of figures. There had been no disorientation for external space and the only disorder in the sphere of the body-image was that he could not visualize parts of his body.

Investigation of this patient's powers of visualization revealed that they were greatly influenced by opening the eyes. As he had stated that as soon as he shut his eyes he could not see anything at all, he was asked to close his eyes and then try to visualize his house. He then said: "I know that there is a house in the road there, a semi-detached house. It's a terrible strain to picture, because no picture comes". He was then told to open his eyes and continue to describe his house and he then said: "It is semi-detached, white stucco on the right and virginia creeper with a green door and bow windows." The experiment was repeated and he was asked to close his eyes and try to visualize his wife's face and he said: "Only an impression, a quick impression, and it's gone as soon as it comes." He was then asked to do the same with his eyes open and he said "Oh, she's full-faced with greying

hair, heavy eyebrows, grey-blue eyes, a retroussé nose and full mouth." He then said: "Everything is more easy with the eyes open without exception." He was then asked to close his eyes again and describe his own foot. He said: "I can't see a foot: I can't visualize anything at all when my eyes are shut." He was then asked to open his eyes and promptly described a naked foot in detail. He had no aphasia or agnosia. His answers in the 100–7 test were correct. He was able to repeat 7 digits forwards and 4 backwards, and he succeeded in repeating a Babcock sentence accurately at the second attempt.

Routine examination revealed no abnormality in the fundi, visual acuity, visual fields or central nervous system elsewhere.

The patient was seen again six years later and his condition in respect of the symptoms described was unchanged. Six months previously, however, he had been admitted to a mental hospital on account of an attack of depression for which he had been treated with electrical convulsant therapy and modified insulin treatment. When I saw him on the second occasion he was again depressed and I admitted him to hospital with a view to treatment and in the hope of carrying out further investigations, including electro-encephalography. Unfortunately, however, he became worse and had to be certified. He was sent to a mental hospital, where he was subsequently regraded as a voluntary patient, and one day he walked out of the hospital without giving notice and was later found dead on the railway line.

The two patients whom I have described present more features of theoretical interest than it is possible to discuss fully now. Loss of visualization is usually found in association with other forms of higher visual disability; Charcot's patient, for example, suffered from word-blindness—but only when it is encountered in relative isolation can its nature be investigated. The suggestion was made in the case of my first patient that it might be a neurotic symptom, and my second patient suffered also from psychotic depression. But my first patient had in no way a neurotic personality and I do not believe that so clear-cut a syndrome, characterized by symptoms possessing no conscious relationship to each other, and occurring in every case after organic lesions of the brain, is other than organic in origin.

If this be accepted, the main interest of the syndrome is psychophysiological. The loss of visual imagery was more complete in Case I than in Case II, in whom visual images sometimes occurred spontaneously though in an impoverished form, and not under the control of the will. The patient exhibited a striking enhancement of visualization when his eyes were open, as though stimulation of the visual cortex strengthened visual imagery. It is unfortunate that this could not be tested electro-encephalographically. In Case I there was an asymmetry in the response to photic stimulation.

Perhaps the most surprising feature is how little the loss of voluntary visualization impaired functions in which visual imagery might have been expected to play some part. Thus, patient No. 1 had a normal memory span for visual objects and could draw designs and describe pictures from memory. Similarly, though he could not visualize parts of his body, he could chart a point touched upon an outline drawing of the body. Charcot's patient showed the same features. It would seem, therefore, that a patient who has no power of voluntary visualization can, nevertheless, recognize objects and persons, accurately propositionize about them, as Hughlings Jackson might have put it, and also reproduce objects graphically. It follows that visual imagery is not essential to these processes, which therefore must depend upon neurophysiological schemas which do not themselves enter consciousness. And the same is true of dreaming, which in patients who have lost the power of visualization continues without visual images.

What, then, is the value of visual images? The image, whether visual or otherwise, in so far as it is a representation of an object reproducible at will, has the great value of enabling thought to deal with the object in its absence, and the visual image being spatially extended has the special advantage of facilitating imagined action in space. Its function, in fact, is well illustrated by the hampering effect of loss of visualization upon the builder designing a house.

My patients throw no light upon the situation of the lesion responsible for the loss of visualization, but there is some evidence suggesting that it is probably in the parastriate region.

REFERENCES

CHARCOT, J. M. (1889) Clinical Lectures in Diseases of the Nervous System. London; **3**, 151.
WILBRAND, H. (1892) *Dtsch. Z. Nervenheilk*, **2**, 361.

## Basilar Artery Stenosis and Thrombosis

By J. L. SILVERSIDES, M.D.(Can.)
*Toronto*

### INTRODUCTION

INTEREST in arteriosclerotic brain disease has been increased, or revived, in recent years for several reasons. These include the common use of arteriography, newer physiological observations of cerebral circulation, and the increased recognition of carotid artery occlusions. Verification by angiography of arteriosclerotic stenosis and thrombosis of the internal carotid artery has been

frequent enough to give fairly clear understanding of the related clinical symptoms. We have come to appreciate the occurrence of quite focal signs in this condition, signs formerly thought indicative of small vessel occlusion on the basis of thrombosis, vessel spasm, or the rupture of small miliary aneurysms. The symptoms of arteriosclerotic basilar artery stenosis, comparable to carotid stenosis, are much less clearly worked out. It is unlikely that arteriographic confirmation will ever be common enough in this area to answer our questions. It would seem reasonable to approach this problem by considering the antecedent cerebral symptoms in cases of basilar thrombosis.

## Method and Material

It has been our plan to study basilar stenosis by surveying in detail the symptoms antedating thrombosis of the basilar artery and its main branches. This preliminary report is limited to consideration of confirmed cases of basilar artery thrombosis. 22 such cases are here reported. 16 cases occurred in Sunnybrook Hospital, Toronto, between the years 1946 and 1952; 6 cases are from the Toronto Western Hospital between the periods of May 1951 and May 1953. 13 of the 22 cases presented the fairly typical clinical picture of basilar artery thrombosis. The remaining 9 cases were of special interest regarding their pre-thrombotic symptoms. These symptoms included disturbances of consciousness, dysarthria, mutism, hemiplegic manifestations, vertigo, tinnitus, &c.

## Description

*General* (22 cases).—19 patients were male, 3 were female. The age range was 47–81 years, with an average of 66 years. 14 patients were hypertensive; 6 had normal blood pressure prior to their terminal illness; the remaining two cases showed marked hypotension with no record of previous average blood pressure.

*Group I* (13 cases).—These showed the more typical clinical picture of basilar artery thrombosis. There was sudden onset of loss of consciousness, either as the presenting symptom or closely following brief initial symptoms such as severe generalized weakness, frontal headache, vertigo, dysarthria, vomiting, or hemiplegia. Coma usually developed rapidly and persisted, and death followed in from one to eight days. Flaccid quadriplegia was the initial finding in 4 of the 13 cases. In 7 cases early examination revealed signs of hemiplegia but this only preceded quadriplegia for periods up to twenty-four hours. One patient had 3 transient episodes of right hemiplegia in the nine days prior to his terminal sudden loss of consciousness and quadriplegia. The remaining patient was admitted in coma but a history was obtained of forty-eight hours' duration. This patient began with hemianæsthesia for twelve hours, hemiplegia in addition for the next twelve hours, and on the day before coma developed he was also incontinent and dysarthric but quite conscious. Accurate history of recurrent premonitory symptoms was not obtained in this group as they were admitted to hospital in coma. Pathological examination in this group revealed thrombus formation in the proximal portion of the basilar artery in 6 cases and in these oculomotor palsies or ophthalmoplegia were noted in all. In 7 cases the distal portion of the artery and the vertebral arteries were involved in the thrombus formation.

*Group II* (9 cases).—These cases had recurrent premonitory symptoms prior to terminal basilar artery thrombosis that suggested periodic insufficiency of blood flow to the brain-stem. Stenosis of the basilar artery occurred so frequently in the whole series that it suggested that it was a causal factor in the terminal thrombus formation. With basilar stenosis as the underlying cause, the immediate cause could well be temporary lowering of blood pressure occurring in hypertensive, normotensive, or even hypotensive individuals. Brief comment of some premonitory symptoms is recorded.

(*a*) *Disturbances of Consciousness*

A 59-year-old man was perfectly well until ten days prior to death when he developed brief episodes of loss of consciousness, associated with transient paralysis of the left arm and leg. Between these episodes the patient was alert, cheerful, well oriented with no specific complaints. He walked into hospital on the day prior to death but the following morning was discovered to be mute and extremely weak, although aware of his surroundings and responding to commands. Eye movements were normal. Shortly afterwards he suddenly became unconscious; a right facial weakness was evident and quadriplegia was present with spasticity a little more marked on the left. Bilateral lower limb clonus and Babinski responses were also present. He died the same evening, but four hours prior to death he developed status epilepticus that could not be controlled. Post-mortem revealed marked atherosclerotic stenosis with a recent thrombus occluding the whole length of the basilar artery.

Derangements of consciousness and their relationship to brain-stem lesions have evoked considerable attention in recent years. It has been shown that lesions anywhere in the brain-stem can cause disturbed consciousness. Tumours, hæmorrhages, concussion and other factors have been widely studied. From case reports it is apparent that the liability to unconsciousness in brain-stem lesions varies with, among other things, the rapidity with which the lesion develops. Temporary ischæmia as one of the causes of intermittent attacks of unconsciousness appears a logical concept. We feel that atheromatous stenosis of a vessel lumen sets the stage for these intermittent episodes to occur.

The concept of a waking centre and the introduction of the term parasomnia to denote damage resulting in a "mixture of sleep and illness" is well known. Anatomical localization of such a centre is still unsure but the reticular formation in the medial tegmentum of the mid-brain is attracting most attention at the present time. Extensive areas of softening in the brain-stem, occurring without alteration of consciousness, have been evident to pathologists for many years. However, when a large area is temporarily deficient in blood supply and collateral circulation is poorly developed, the situation is apparently not comparable. The degree to which consciousness is altered is extremely variable and may persist for long periods.

Six months prior to death a 62-year-old housewife noted frequent transient attacks of blurring of vision of both eyes, generalized weakness, and brief paræsthesiæ in the left hand. One month prior to death, left frontal headache, vertigo, and tinnitus occurred which was persistent and increasing in degree. Teichopsia was an occasional complaint. Fourteen days prior to death she became bedridden and exhibited a pathological desire for sleep, and terminally was sleeping most of the day and night and difficult to arouse. A few days later, difficulty in swallowing was apparent and she became increasingly unresponsive. On examination her blood pressure was 130/75, she responded to painful stimuli only, the left corneal reflex was absent and there was left facial weakness and a right Babinski response. Terminally there was flaccid quadriplegia, contracted pupils, and deep coma. At post-mortem there was extreme atherosclerosis and stenosis of the basilar artery with recent thrombus formation. The right vertebral artery showed both old and recent thrombi and the left vertebral artery contained a partially occluding recent thrombus.

A 69-year-old hypertensive male had had three episodes of right hemiplegia in a five-year period prior to his death. All episodes had cleared with minimal residua. One month prior to death he developed incontinence and three days later developed a flaccid quadriplegia with bilateral Babinski responses. At this time he lapsed into a somnolent state from which he could be aroused with increasing difficulty. This state lasted for thirty-two days with terminal deep coma. Post-mortem revealed old and recent pontine softenings, extensive basilar artery stenosis and thrombosis. No cerebral pathology was evident.

Thus, while these patients invariably die in coma we may have a variety of experience in respect to their states of consciousness in the pre-coma stage of their illness.

(*b*) *Dysarthria and Mutism*

Dysarthria is one of the commonest symptoms in both severe classical cases and also in the intermittent episodes preceding basilar thrombosis which seem to be the result of transient anoxia of the brain-stem. Mutism can occur alone, develop on dysarthria, or it may be seen with hemiplegic symptoms and signs. We do not feel the mutism is necessarily anarthria or indeed that it is due to pseudobulbar palsy, and bilateral involvement of the cortico-bulbar tracts in each case would hardly seem a rational explanation. We do not feel it is transient motor aphasia. A relationship might be contemplated to that state called akinetic mutism because of the frequently associated intermittent complaints of profound weakness. We feel this symptom is not clear in terms of its pathophysiology and certainly merits reconsideration in cases coming to attention.

A 63-year-old widow developed episodes beginning with paræsthesiæ of her upper lip and right hand, and a sensation of heaviness in the right arm and leg. Almost immediately she experienced extreme coldness of the tip of her nose, her upper lip, her right hand and her right foot. She was quite mute and unable to utter any sound, she could still move her limbs and never lost consciousness. Months later these attacks became associated with uncontrollable weeping but pathological laughter was never present.

A woman patient developed episodes of vertigo, uncontrollable rolling conjugate movements of her eyes, and paræsthesiæ of her left arm and right leg. The paræsthesiæ were accompanied by weakness of these limbs. The attacks were brief, lasting 30–60 seconds but became progressively longer with the months. One year later they lasted up to fifteen minutes and at that time she developed complete mutism for the whole episode, followed by normal speech.

(*c*) *Pontine Hemiplegia*

Hemiplegia as an initial symptom occurs very frequently. This may be transient, or may be severe and quickly followed by quadriplegia. There may only be weakness and heaviness experienced in the arm and leg. Where crossed hemiplegia occurs a localization appears certain. Hemiplegia of an arm and leg, almost equally affected and without facial involvement, suggests possible thrombosis of a vertebral artery. Further, if on the dominant side and involving face, arm and leg, without sensory or speech disturbance, and with early and severe spasticity then the lesion is suspected as being in the anterior pons. Penetrating branches of the basilar artery are known to come off at right angles. The origin of these vessels may be affected by severe atheroma or thrombosis. Thrombus formation is probably lateralized early and this may account for the initial hemiplegic findings. Anatomically we might expect to see an occasional bilateral anterior pontine softening resulting in a paraplegia or quadriplegia.

A 76-year-old man with normal blood pressure had a sudden attack of vertigo and loss of consciousness three years prior to death. He was then apparently well for about one year when he developed a slowly progressive spasticity of both legs and a little more marked on the left. He became incontinent of urine. Over the next two years he had repeated transient attacks of acute vertigo associated with severe generalized weakness. Terminally signs of spasticity occurred in both arms. Three days prior to death he developed a series of "tonic fits" and death occurred with hyperpyrexia. At post-mortem there were old and recent softenings in the pons, most marked anteriorly, and the degree of stenosis of the basilar artery was remarkable. There was recent thrombus formation. No other pathology was found to account for the symptoms.

(*d*) *Vertigo and Tinnitus*

These symptoms occur so frequently that it suggests that Deiter's nucleus is the most sensitive mechanism in the pons to react to transient anoxic effects. We have not encountered decrease of acuity of hearing or deafness as a complaint. When vertigo and tinnitus occur suddenly, are persistent, or even increasing in severity they appear to constitute a bad prognostic feature. In one patient briefly mentioned in respect to pathological somnolence, she voluntarily retired to bed in her terminal illness because of persistent and increasing vertigo, buzzing tinnitus, and teichopsia. In typical basilar artery thrombosis a frequent history is of a sudden onset of profound weakness, acute vertigo, nausea and vomiting and then coma developing.

(*e*) *Miscellaneous*

Brief attention is drawn to several other features of interest.

(1) *Epilepsy.*—This was seen in 3 cases. All were in deep coma. 2 showed "tonic fits" that were mistakenly labelled decerebrate rigidity by the house staff. One already mentioned had terminal status epilepticus. Epilepsy only appears to occur in the terminal phases.

(2) *Paræsthesiæ.*—Lateralized sensory disturbance of lip, hand and foot occurred in 3 cases in early symptomatology. This has been previously recorded. Paræsthesiæ of the trunk did not occur, hemianæsthesia was noted in one case only. The lateralized sensory complaints, particularly if accompanied by visual symptoms, are almost indistinguishable from those seen in migrainous aura.

(3) *Weakness.*—The most frequent subjective sensation experienced by these patients was a feeling of profound weakness. While observations are inadequate this did not appear to parallel blood-pressure variation. A profound vasovagal mechanism suggests itself.

(4) *Behaviour.*—Abnormal behaviour occurred occasionally in these patients. This included amnesia, hysterical patterns, transient paranoid reactions, noisy confusion and personality regression. Some cases suggest a possible thalamic involvement from interference with blood supply but this remains speculative.

### Conclusions

The usual clinical presentation of basilar artery occlusion by thrombosis and embolism is well known and allows ante-mortem diagnosis. The clinical variants dependent on the site of occlusion being proximal or distal in the vessel are also understood.

The usual assumption as to the cause of isolated or repeated vascular brain-stem lesions has been occlusion of penetrating pontine branches of the basilar artery. We would suggest that in certain of these cases, the symptoms occur as a result of stenosis of the basilar artery, in a similar fashion to that seen in carotid stenosis.

The symptoms preceding thrombosis of the vertebral and posterior inferior cerebellar arteries may have similar implications.

Arteriosclerotic stenosis of larger cerebral arteries is probably more important than has been shown in causing minor cerebral attacks.

Basilar artery stenosis as a cause of brain-stem symptomatology is probably more common than is generally appreciated.

## Pure Word Blindness Considered as a Disturbance of Visual Space Perception [*Abridged*]

By J. Purdon Martin, M.A., M.D., F.R.C.P.

(1) Pure word blindness is a condition in which the patient is unable to read, though showing no signs of aphasia. The fact that he is able to write shows that he has not lost the memory of the word forms or of their symbolic meaning. What he has lost is the ability to recognize the word forms, and because of this he cannot read even his own writing.

(2) In cases of gross disturbance of visual space-perception of the kind described by Holmes and Horrax the patients are unable to read, but if the postural sense is normal in the patient's right hand he is able to write. He thus presents the essential features of pure word blindness. Such a patient is unable to locate objects in the field of vision or marks on a paper in front of him, he is unable to draw a line between two points, or to see the relations of lines to each other. He has lost what may be called his visual geometrical appreciation or visual geometric sense.

Since I became aware in 1938 of this variety of word blindness I have not seen any case of pure word blindness in which there were not also disturbances of visual space appreciation of geometric type.

(3) Letters and words are geometric formations and are arranged geometrically in lines and pages. For instance each of the letters A, H, K, N, F, Y consists of three short lines, in different geometrical relationship to each other. The child when he goes to school has to learn to recognize these forms and to discriminate between letters of similar form such as M and N, M and W. As he does so he is cultivating his visual geometrical appreciation. Later he learns short words and they become

recognized as geometrical forms in themselves. As he reads sentences of the type "A CAT SAT ON A MAT" he is learning to discriminate between similar geometrical formations. When he learns long words, they are, of course, geometrical units too, but may be read in syllables or other parts as compound geometrical forms. Over a period of years he cultivates this appreciation of specialized geometrical forms to its highest pitch and becomes able to scan lines and pages and almost unconsciously to recognize the varied word forms that are presented to his sight. This probably represents the highest development of the appreciation of spatial relationships by sight.

(4) It is very interesting to review recorded cases of pure word blindness and also those of one's own experience, with these considerations in mind. In all the fully described cases it is apparent that other disturbances of visual geometrical appreciation were present, but only a few examples can be given.

In Déjerine's classical case the patient before the onset of his disability had been a very neat writer, but when he had become word-blind, although he could write freely, his writing had lost its former neatness, the lines were often sloping and the words irregularly spaced, and also the writing was larger and the letters less regularly formed. Déjerine made the observation (as did Bastian in a similar case) that the patient could write as well with his eyes closed as with them open, which shows that he had lost all the visual geometrical control normally exercised when writing.

In Holmes' recent case the patient could write but if he raised his hand which held the pencil from the paper, he was unable to locate exactly the position from which he had left off and so unable to continue on the same line. He also made mistakes in telling the time due to failure to appreciate correctly the relative positions of the hands on the dial of the clock.

Many other examples might be cited, and one is bound to conclude that pure word blindness is accompanied by other disturbances of visual geometrical appreciation and is part of a larger disturbance belonging to the sphere of spatial appreciation.

(5) Conversely, a relatively slight disturbance of visual geometrical appreciation causes an inability to read. This is a familiar experience to those who have optical refractive errors of any considerable degree and are consequently dependent on glasses for reading ordinary print. When he takes off his glasses the person with a refractive error has a general disturbance of visual geometrical appreciation, but the outstanding disability, as a rule, is that he cannot read. He can write, but not as well as with his glasses on and he cannot read what he has written. He is thus suffering from a variety of pure word blindness. If he engages in other delicate activities he soon becomes aware of the general nature of his visual disturbance, but for all larger activities his geometrical appreciation is adequate.

Judging from the descriptions the functional condition of some patients with pure word blindness, e.g. Holmes' patient, was not very different from that of many persons with refractive errors when deprived of their glasses.

(6) Cases of pure word blindness differ in severity and, in fact, it may be that there are as many degrees of dyslexia (of central origin) as there are of optical refractive errors.

The cases of gross visual disorientation represent the most severe degree. The patient is not merely unable to read but cannot even locate the sight-testing card. (In such cases the lesions are bilateral.) In the more usual cases the patients have no gross disorientation but are unable to read letters, words, figures or music: they can write but may write as well with their eyes closed, as with them open, i.e. they exercise no visual geometrical control. Others retain a considerable degree of visual geometrical control of writing. Some patients, though unable to read letters or words may read arabic numerals, others again may be able to read musical notation (an obvious geometrical formation); some who are unable to read letters may recognize a number of individual word forms, some may be able, more or less, to read familiar handwriting. All have difficulty in copying, but the degree of difficulty varies. All these variations are probably matters of degree and may be matched by the varied abilities of persons with slightly different refractive errors. If they are matters of degree they must depend on slight variations in the extent of the lesions of the appropriate structures in the dominant hemisphere. On this supposition arabic figures may be read in some cases, because they are very simple geometrical formations and being fewer in number require less discrimination than letters. An alternative suggestion is that the ability to read figures but not letters or words is due to the memories of these formations being stored in a different part of the brain from that concerned with the memory for word and letter forms. The former explanation seems to me the more acceptable, and Alexandra Adler has taken the same view. It must also, however, be taken into consideration that the degree of residual function in a case of pure word blindness with a lesion in the dominant hemisphere, depends not only on the residual function of the damaged parietal lobe (or its connexions) on the affected side but also on the functional abilities of the corresponding structures in the other hemisphere. In a recent case an operative lesion had to be made in the left parietal lobe and the patient immediately afterwards showed severe disturbances of parietal lobe function, including complete alexia, but he was, nevertheless, able to recognize elementary geometrical forms such as a triangle, a circle and a square, and it seemed to me most likely that this ability was attributable to the function of his intact right hemisphere.

While on the subject of variations it should be mentioned that in some cases, which are almost

pure, an element of language disturbance may nevertheless be present, i.e. they are really "mixed" cases.

(7) The deaf and dumb language is another system of communication that is dependent on geometrical forms and therefore requires geometrical appreciation on the part of the reader. Braille is a geometrical system that is read by touch, and therefore depends on the somatic space-appreciation sense. We can develop codes or systems of communication of greater or less delicacy (e.g. Morse code) making use on the receptive side of any of our sensory modalities, and it is obvious that any one of them can be effective only if the sensory modality concerned is intact. Apart from spoken speech, the system that we have developed most highly (writing and reading) is one that is based on the visual appreciation of geometrical form and in order that it may function properly the receiver's visual geometrical appreciation must be adequate.

## Post-encephalitic Mental Paroxysms

By J. ALLAN WALTERS, M.D., D.P.M., F.R.C.P.(Can.)
*Toronto*

ENCEPHALITIS LETHARGICA may leave in its wake abnormal mental states which are entirely periodic and often in association with oculogyric crises. They were first observed by Wimmer (1926) and Holmes (1928) and Williamson-Noble (1928), and have since been found to involve awareness, perception, feeling, thinking and behaviour, in various combinations (von Economo, 1931; Rosner, 1942; Schwab *et al.*, 1950).

In the mental paroxysms of 16 post-encephalitic patients who have been followed over thirteen years at the Toronto General Hospital, the following critical features have been observed:

(1) The mental paroxysm may occur apart from as well as with, the oculogyric crisis, and apart from Parkinsonism.

(2) The mental disorder consists of an arrest of the flow of mental life while the patient is held with a more or less fixed mental pattern which cannot be voluntarily shifted. After minutes, hours, or days, the arrest ceases and the mental life again flows on in its normal changing way.

Sometimes trick methods may be found to break up this stalled mentation, just as tricks may be learned to break up the ocular attacks. The patient or others may be able to manœuvre some special object or topic or situation into the foreground of attention and bring a release.

(3) The mental state during the paroxysm may be: (*a*) a discrete arrest of the flow of affective patterns with the mind fixed in a state of anger, fear, or depression.

(*b*) A discrete arrest of the flow of thinking with the mind fixed and compelled to dwell upon one topic in an obsessional way.

(*c*) An incongruous arrest of thinking and feeling at the same time. Feeling may be fixed in sadness while thinking may, with no appropriate mood, be held revolving around a point in a "folie de pourquoi" fashion.

(*d*) The flow of perception may be discretely arrested with persistent colours or musical tunes lingering on an otherwise changing perceptual field. Time and space perception may seem to arrest—as if time had stopped—or as if the person was alone in infinity. Perception of reality may arrest with the patient left in a state of "double consciousness" (Wilson, 1928) wherein the conscious patient behaves to a false world of memory and mental imagery.

(*e*) Adaptive behaviour may be arrested and the patient is little able to deal with new situations appropriately. More automatic movements and speech may be fairly preserved or may be stalled.

(*f*) The voluntary capacity to change a new visceral situation may be lost, with the patient unable to open bowel or bladder during a paroxysm.

(4) The oculogyric attack consists of the eyes held more or less in one position. A posture is maintained and the capacity to range and explore visually is lost during the crisis. This is not a forced movement but a forced posture. The truth of this is best seen in those rarer crises where the eyes persist in falling into the shut position and in those where the eyes lock centrally in a fixed stare.

(5) The ocular attack and the mental attack, when associated, usually start and stop together. The temporal relationship is often so close that one feels safe in supposing that the fundamental disorder is of some physiological process common to both ocular and mental adaptation and necessary in changing the locus at which a particular function may operate. While disordered, the patient is unable to change an oculomotor position and explore. At the same time, he is unable to change a mental pattern and adapt to the flow of his current of experience.

### DISCUSSION

From these critical features it is suggested that the essential disorder is a loss of the capacity to change to a new position and there to use a needed pattern of action. This is a loss of some very essence of adaptive capacity.

Successful adaptation is an integrated procedure that includes a differential function for change

of locus as well as a differential function for doing what is needed at the new point. In these post-encephalitic patients, when they are not fixed at a point, there seems to be no derangement of their ability to think or feel or look about. The disorder does not seem to be within those simpler representations of function which we find damaged by local lesions of the cerebral cortex. It seems to be a disorder with the patterns of action intact and the patient at times being unable to use them. This seems to be a disorder of re-integration of specific representations of function at a level where they are re-represented within the neural action that attends conscious adaptation. This would be (according to Jackson, 1931) at the highest neurological level.

The disorder reminds one of a flow of traffic with a signal system for stop and go. When the regulatory mechanism goes awry, the red light stays on with the green light off, and no change of flow to new positions occurs. Now the loss of the capacity to change is a disorder of timing for change. There seems to be a disorder of those neural mechanisms essential to inhibit one pattern of neural action and excite a new pattern of neural action. This loss of timing mechanisms may involve voluntary or involuntary function. The loss may be very discrete and limited to ocular or mental or part of the mental life only, or it can be multiple in both congruous and incongruous combinations. This is a loss of very specific and organized function. It suggests an effect of the encephalitic process upon some timing mechanisms so arranged as to allow highly selective damage. Such a delicate selection requires an arrangement of timing mechanisms within the central nervous system that provides for discrete and specific physiological and, possibly, anatomical organization.

With the oculogyric crises and the mental paroxysms reduced to a common type of disordered timing mechanisms at a neurophysiological level, it is difficult to proceed further since our knowledge of the physiology for the timing of action is so scanty.

Beevor (1904) followed Jackson in his contention that cortical motor representations intrinsically contained the process of timing for those changes which permit a sequence of muscular action to change the position of a limb around a joint. But in the post-encephalitic patients it seems that the defect is of a higher order where the need is to change from action at one point to action at a new point. Is this simply a more complex ordering of intrinsic timing mechanisms within cortical re-representations? Or could it be that timing mechanisms are arranged in some way apart from representations of specific function so that specific neural action can be aroused or inhibited for integrated or differentiated function? This might be possible if there were anatomical arrangements for the special function of timing with both diffuse and specific connexions to other parts of the brain. The new knowledge of the reticular substance illustrates such an anatomical arrangement with diffuse and specific projection pathways for general or particular arousal and inhibition. One is left wondering if timing mechanisms might not be represented likewise in some central structure with a regulatory control over the flow of particular and specific action. Such an arrangement seems almost necessary to account for the delicate and selective disorder that is produced by the encephalitic process.

## REFERENCES


Beevor, C. E. (1904) Muscular Movements and Their Representations in the Central Nervous System. London.

Economo, C. von (1931) Encephalitis Lethargica. Oxford.

Holmes, G. (1928) *Proc. R. Soc. Med.*, **21**, 994.

Jackson, J. Hughlings (1931) Selected Writings, Vol. II. London.

Rosner, A. A. (1942) *Amer. J. Psychiat.*, **99**, 224.

Schwab, R. S., Fabing, H. D., and Prichard, J. S. (1950) *Amer. J. Psychiat.*, **107**, 901.

Williamson-Noble, F. A. (1928) *Proc. R. Soc. Med.*, **21**, 987.

Wilson, S. A. K. (1928) Modern Problems in Neurology. London.

Wimmer, A. (1926) *Acta Psychiat. Kbh.*, **1**, 173.


**W. Ritchie Russell,** C.B.E., M.D.—A Study of Muscle Recovery After Poliomyelitis. This paper has been published in *Lancet*, 1954, i, 330.

## President—E. A. Carmichael, C.B.E., F.R.C.P.

[*November 5*, 1953]

### Meeting Held at the National Hospital, Queen Square, London, W.C.1

**Cortical Blindness and Spastic Quadriparesis Following Apnœa in an Asthmatic Attack.**—J. Foley, M.D., M.R.C.P. (for J. Hamilton Paterson, M.D., M.R.C.P.).

M. N., female aged 25, asthmatic since childhood.

22.6.53.—Admitted to hospital cyanosed after a day in status asthmaticus. A period of apnœa lasting two to four minutes was accompanied by a convulsion, but gasping respiration had started again by the time she was given intravenous aminophylline. Blood pressure 155/105. Bronchospasm diminished with ACTH. For twelve days she remained stuporous and restless with involuntary movements of the jaw and shoulders and a spastic quadriplegia more marked on the right side. Sixteen

days after the onset she could not speak but could respond to commands and raise her arms above her head, but in the next two weeks she became noisy and was transferred to an observation ward.

29.7.53.—Admitted to Atkinson Morley's Hospital. Conscious; no impairment of comprehension of speech; amnesia for whole illness; Gerstmann's syndrome. Speech grossly slurred and almost unintelligible. Vision amounted to perception of light only. Fundi and pupils normal, external ocular movements full. Constant grimacing, rolling of head and torsion movements of shoulders. In addition to severe spastic quadriparesis there was bilateral wrist drop and considerable wasting of the forearm and hand muscles, with loss of joint sense in the hands and impairment of light touch on the fingers only. The EEG consisted of virtually straight lines; lumbar encephalogram normal.

In the next two weeks there was considerable improvement. She had almost constant formed, coloured visual hallucinations of patterns, jewels and toys; though on one occasion she had an hallucination of the Royal Family she was unable to visualize her relatives or any object at will, and she no longer dreamed. Visual fields tested with a beam of light were full, with no definite central defect; she had fragmentary vision for moving objects and bright colours. Audiometry was normal. Apart from dysarthria speech was unaffected. She had a retrograde amnesia of eight months. The athetosis, wrist-drop and wasting of the hands disappeared, but spastic quadriparesis with cerebellar ataxia persisted; sensory loss was confined to joint sense and two-point discrimination in the hands. This stage was reached four months after the onset. On 20.10.53 she had three fits, after which vision deteriorated and hallucinations vanished.

### Comment

Improvement in cases of cerebral damage due to anoxia is rare, though it is seen in cases of carbon-monoxide poisoning. The damage here affected the parieto-occipital and motor areas, basal ganglia, cerebellum and peripheral nerves. Destruction of anterior horn cells in the cord has been found in fatal anoxic cases, but peripheral neuritis has so far been reported only in cases of carbon-monoxide poisoning. The improvement in this patient's cerebral signs coincided with the disappearance of wasting in the hands, and much of the earlier cerebral deficit may have been due to demyelination rather than to neuronal damage.

### BIBLIOGRAPHY

DOUGLAS, A. J. (1949) *Canad. med. Ass. J.*, **61**, 123.
HAGLUND, C. (1951–2) *Acta chir. scand.*, **102**, 364.
HOWKINS, J., MCCLAUGHLIN, C. R., and DANIEL, P. (1946) *Lancet*, i, 488.
WILSON, G., and WINKELMAN, N. W. (1925) *Arch. Neurol. Psychiat., Chicago*, **13**, 191.

**Cerebral Anoxia Following Burns.**—J. HAMILTON PATERSON, M.D., M.R.C.P.

A. J., male, aged 4. Admitted to hospital on 11.9.51 with extensive burns acquired when his night attire caught fire. Although his general condition was fair he had widespread burns over the front of the chest, abdomen and thighs. Six hours after injury he collapsed with a rapid feeble pulse and an hour later he had several convulsions which were eventually controlled with Pentothal. He had a further seizure on the third day and thereafter he was nursed in an oxygen tent. He began to take fluids by mouth, but that evening his temperature rose to 106·2° F. and his respiration rate to 96. On the next day further fits were controlled with paraldehyde, but two days later he was found to be unconscious with widely dilated pupils and spastic extremities. Subsequently his general state remained unchanged although he had no further convulsions. He had to be fed by a nasal tube.

On his first admission to the National Hospital six weeks after injury he was found to be entirely inaccessible. Occasional twitching of the face and limbs was seen but otherwise he lay immobile. He appeared to be blind and deaf but he responded slightly to painful stimuli and he showed sucking and chewing reflexes, while the corneal responses were likewise present. Both pupils were widely dilated and did not react to light. The optic discs were pathologically pale with clear-cut margins. All four extremities were extremely spastic, the right arm being held in a flexed and adducted position, the left being extended. Both legs were fully extended. Two years later, on his second admission, his general state is much the same and he does not appear to have grown much in the interval. Usually he lies quite still sucking his fingers, though he becomes restless when disturbed and cries and grunts for a while. He is now taking food by mouth but only with difficulty. He is still quite blind but he can now hear to some extent as he can be startled by a loud noise. His limbs are much less spastic, the arms being held flexed and the legs extended. The tendon reflexes are very brisk and he has bilateral extensor plantar responses.

*Investigations*

*On first admission.*—Blood count: moderate microcytic anæmia. Urine and cerebrospinal fluid normal.

Caloric responses roughly normal. EEG "that of an unconscious patient, quite unspecific in its nature."

Air encephalograms: gross generalized dilatation of the whole of the ventricular system.

*On second admission.*—Bilateral carotid arteriograms; normal.

COMMENT

It must be very rare for a child of this age to survive such severe cerebral damage for he has virtually become decerebrate. His peripheral blindness is of interest as most cases with loss of vision following anoxia apparently have normal fundi and pupillary reactions. His type of blindness is that which is occasionally seen following severe hæmorrhage.

**Norman's Type of Diffuse Sclerosis.**—DENIS WILLIAMS, M.D.

A girl of 11, with normal parents, has been studied in the National Hospital, Queen Square, since the age of 5 when she began to show disorders of movement. The condition has steadily advanced and there is now generalized and severe dystonia with intellectual defect.

Brain biopsy performed by Mr. Wylie McKissock led to histological study by Dr. William Blackwood, who showed slides typical of diffuse sclerosis of Norman's type. The case will be reported in detail when more facts are known about it.

**Glomus Jugulare Tumour Presenting with Papillœdema and Obscurations of Vision.**—RAYMOND HIERONS, M.B., M.R.C.P. (for S. P. MEADOWS, M.D., F.R.C.P.).

Mrs. A. N., aged 38, admitted to the National Hospital with a history of frontal headaches of three months' duration and attacks of blurred vision. She denied any other symptoms, especially deafness, vertigo or bulbar symptoms.

The only relevant feature in the past history was a discharging left ear in childhood. The family history was negative. (Examples of familial cases of this condition are, however, described in the otological literature.)

Examination revealed that intelligence was slightly below average but no evidence was noted of deterioration and speech was normal. Other abnormal signs included:

Moderately severe bilateral papillœdema with hæmorrhages and exudates. Slight left-sided deafness.

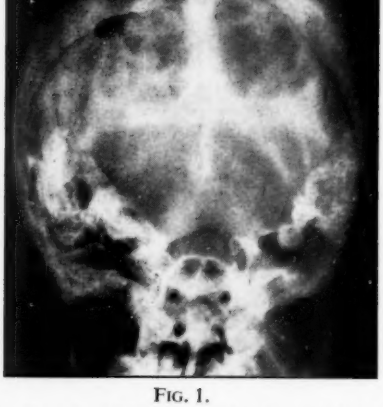


FIG. 1.

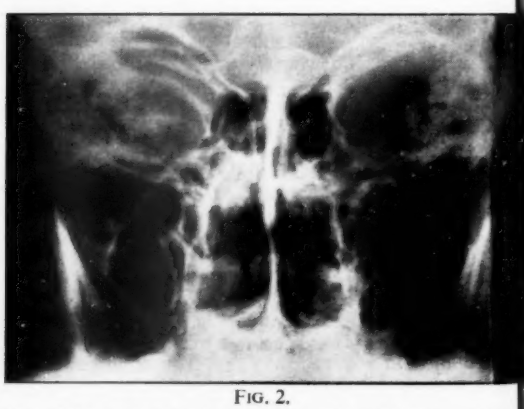


FIG. 2.

FIGS. 1 and 2.—X-rays showing massive destruction of the apex and inferior portion of the left petrous bone.

First-degree vestibular nystagmus on deviation to the right. Left corneal reflex diminished but otherwise no sensory loss detected on the face. Masseter and temporal muscles of normal power and bulk on the two sides. Slight over-reaction of the left lower face on voluntary movement and probably impaired taste over the left anterior two-thirds of the tongue. Paresis of the left side of the palate and left vocal cord. Normal power of the sternomastoids and trapezii. Very marked atrophy of the left side of the tongue with fasciculation on this side. In the motor system no abnormality of development, tone, power or reflexes detected. Minimal ataxia of the lower limbs, slightly more marked on the left and unable to walk along a straight line. No bruit detected over the cranium. The left auditory meatus seen to be filled by a dark blue vascular swelling which was considered by Mr. Terence Cawthorne to have the appearance of a glomus tumour. X-ray skull (Dr. Hugh Davies) revealed signs of increased intracranial pressure in the pituitary fossa and destruction of the left petrous apex (Figs. 1 and 2) extending into the middle and posterior fossa.

Biopsy of the tumour from the external auditory canal reported by Dr. W. Blackwood as "formed of cells with medium-sized rounded or elongated nuclei surrounded by a considerable amount of cytoplasm, the margins of the cells being generally ill-defined. Most of the nuclei are lightly stained but collections of cells with deeply staining small, rounded nuclei occur. One portion of the tumour consisted of solid alveolar masses of cells surrounded by reticulum. The material has been shown to several pathologists, the opinion being that this is neoplastic tissue, part of which has an appearance compatible with, but not undoubtedly diagnostic of, a glomus jugulare tumour."

In view of the dangers of visual failure a full suboccipital decompression was carried out by Mr. Wylie McKissock, a ventriculogram having previously shown the appearances of a large space-occupying lesion in the neighbourhood of the cerebellopontine angle on the left side.

The chief point of interest of this case is its mode of presentation. Interest in recent years in this type of tumour has been chiefly centred in the aural manifestations and with the exception of a recent paper by Dr. R. A. Henson and his colleagues (1953) few reports have been from the neurological standpoint. These authors did not, however, find papillœdema in any of their cases nor in reviewing the literature. Probably, however, with greater awareness of the condition papillœdema will be not so very rare and since this patient was demonstrated I have been informed of two similar cases.

## REFERENCE

HENSON, R. A., CRAWFORD, J. V., and CAVANAGH, J. B. (1953) *J. Neurol. Psychiat.*, **16**, 127.

**First and Second Division Trigeminal Neuralgia Treated by Intramedullary Trigeminal Tractotomy.**—M. A. FALCONER, M.Ch.

*Case I.*—Miss J. D., aged 52, shop assistant.

*History.*—Since 1931 subject to bouts of typical tic douloureux centred in right forehead and spreading to right side of nose, upper lip, and roof of mouth. Averaged one severe bout yearly. A recent attempt at injecting the gasserian ganglion with alcohol resulted in numbness over lower jaw, but not relief of pain.

*Operation* (March 1951).—Right intramedullary trigeminal tractotomy performed under local analgesia. Region of descending tract of V incised to a depth of 3 mm. at a plane 4 mm. below obex. Smooth post-operative course.

*Follow-up* two years eight months later. Completely free of her old pain, and has no appreciable disability. Occasional tingling sensation over right lower lip related to area numbed by pre-operative gasserian ganglion injection. Not conscious of any alteration in the feeling of her right face, except in a cold wind when temperature is appreciated by left face only.

Shows complete loss of pain and thermal sensibility over right side of face and concha of ear, as well as over right side of tongue, palate, and tonsillar region. Touch spared in these regions. Right corneal reflex present but diminished. No ataxia of limbs.

*Case II.*—Mr. G. K., aged 48, borough engineer.

*History.*—Onset in 1941 of bouts of typical tic douloureux involving first and second trigeminal divisions of left face. Longest spontaneous remission nine months.

*Operation* (May 1951).—Left intramedullary tractotomy performed as in Case I.

*Follow-up* two years six months later. Is likewise free of old pain, and has no appreciable disability. Has had three transient bouts of mild paræsthesias involving left malar region and occasional mild aches in left side of nose.

Shows almost complete pain and thermal loss over left side of face, but with preservation of touch. Similar distribution as in Case I, except that pain sensibility persists in inner side of upper lip, left upper gum in region of incisor teeth, adjacent hard palate, and left side of nasal septum. This latter sparing is unusual, and is presumably accounted for by the premaxilla in its development having been supplied from the right trigeminal nerve alone.

Left corneal reflex present but diminished. No ataxia of limbs. For a short time after operation this patient exhibited also loss of pain and thermal sensibility in right lower limb, but sensibility in the leg is now normal.

### DISCUSSION

This operative procedure was introduced in 1938 by Sjöqvist who advocated incising the descending tract of the trigeminal nerve within the medulla under general anæsthesia and at a level 8 to 10 mm. above the lower end of the 4th ventricle (obex). Since then several surgeons have tried the procedure, and most of those who have written about it have been disappointed in the results. Several have recorded complications such as ataxia of the ipsilateral limbs, paralysis of the vocal cords, and impairment of postural sensibility indicating damage to adjacent structures in the brain-stem, and have also reported that the resulting pain loss has been patchy with consequent partial or imperfect relief of pain. Olivecrona (1942) and Guidetti (1951), however, have written more laudatory accounts.

Four years ago I published a description of the operative technique which was employed in these two cases (Falconer, 1949), and also recorded my experience with 20 New Zealand patients operated on at intervals up to four and a half years. The procedure was of no value for post-herpetic neuralgia, but in the 11 cases of unilateral tic douloureux and 2 of bilateral tic douloureux in which the procedure had been performed, it had conferred uniform and apparently permanent benefit and without untoward complications. Two points seemed necessary for success, namely, that the incision should be at a lower level than that originally recommended, and secondly that it should be performed under local analgesia. By sectioning the descending tract at a level 4 mm. or even lower below the obex as advocated by Weinberger and Grant (1943) the complications listed above could be avoided; and by performing the operation under local analgesia as recommended by Olivecrona (1942) the resulting sensory loss could be checked and the extent of the incision regulated. Further, by pricking the medulla with a needle, the position of the tract can be established prior to the sectioning, because both the pricking and the sectioning cause momentary pain in the face.

These two patients presented are the first to undergo this operation in the Guy's-Maudsley Neurosurgical Unit.

Treatment by alcohol injection of the gasserian ganglion would have completely numbed one side of the face and incurred the risk of corneal ulceration. The ordinary run of patients in whom pain affects the lower half of the face are more readily treated by the usual subtotal sensory-root section, for it is technically difficult to produce pain loss in the lower face by intramedullary tractotomy without incurring a risk of some ataxia of the ipsilateral limbs. But for tic douloureux involving the forehead, and also for tic douloureux in which pain appears on both sides of the face, intramedullary tractotomy is the operation of choice, because both touch over the face and postural sensibility in the masticatory muscles are preserved. Indeed, for the latter indication it is far the most preferable surgical procedure, for the lot of a patient who is bereft of all sensibility in the lower jaw (as after bilateral ganglion injections with alcohol) is a pitiful one.

## REFERENCES

FALCONER, M. A. (1949) *J. Neurol. Psychiat.*, **12**, 297.
GUIDETTI, C. (1951) *J. Neurosurg.*, **7**, 499.
OLIVECRONA, H. (1942) *Arch. Neurol. Psychiat., Chicago*, **47**, 544.
SJÖQVIST, O. (1938) *Acta psychiat. neurol.*, Suppl. 17.
WEINBERGER, L. M., and GRANT, F. C. (1943) *Arch. Neurol. Psychiat., Chicago*, **49**, 665.

**Chronic Respiratory Paralysis due to Poliomyelitis Treated by Positive Pressure Inflation of the Chest.**—R. A. BEAVER, B.M., F.F.A.R.C.S., and R. W. GILLIATT, M.B., M.R.C.P. (for M. KREMER, M.D., F.R.C.P.).

Miss E. H., aged 28. Admitted to the National Hospital on 7.7.53 with a history of fever for four days and headache with neck stiffness for one day. Examination on admission revealed no muscular weakness but lumbar puncture showed 468 cells per c.mm. 93% polymorphs. Weakness was first noted on 8.7.53 in left triceps and was followed by rapidly increasing paralysis of all trunk and limb muscles with failing respiration. No bulbar involvement occurred at any stage but spontaneous respiratory movement was virtually absent by 10.7.53, the patient being unable to stay out of a box respirator for more than 90 seconds.

In twelve weeks only slight recovery of the respiratory muscles has occurred and the patient still becomes distressed after two to three minutes of unassisted breathing. The vital capacity has now reached 250 c.c. and slow improvement continues. The patient has been nursed in a conventional box respirator but frequent periods of positive pressure inflation have been employed from the onset in order to allow the patient to be withdrawn from the respirator for nursing procedures and physiotherapy.

The pneumoflator designed by Beaver (1953, *Lancet*, i, 977) was used in the acute stage with a face mask of the self-sealing type (Goorney, 1953, *Lancet*, i, 422), periods of positive pressure ventilation being supervised by an anæsthetist or resident. For the chronic stage a simple non-adjustable mouthpiece has been introduced (Beaver and Gilliatt, 1953, *Lancet*, ii, 1243), which has made it possible for positive pressure inflation by pneumoflator to be carried out safely by the nursing staff without special supervision.